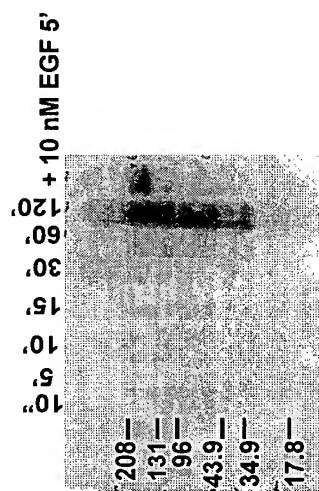


**FIG. 1A**

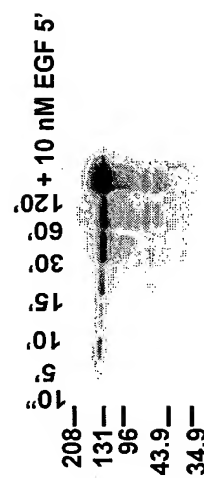
CS-240

**Whole cell lysate/  
anti P-Tyr blot**



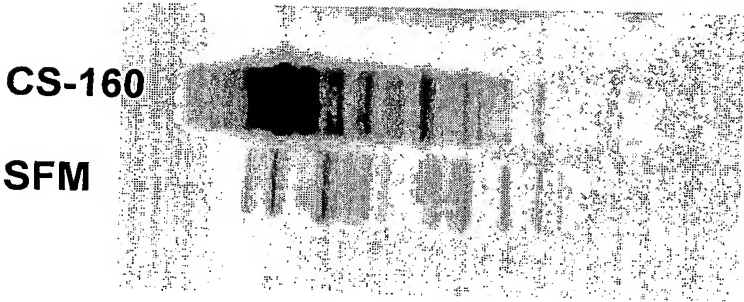
**FIG. 1B**

**EGFR IP/  
anti P-Tyr blot**



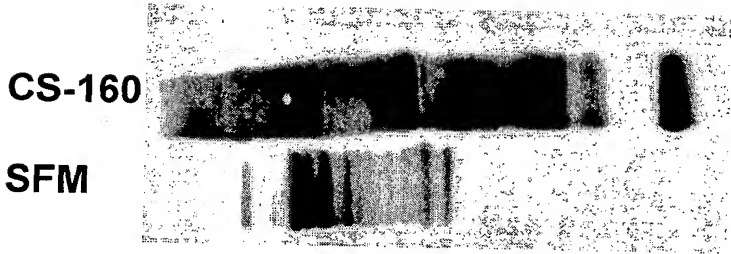
**CS240 = 240 cigarettes/ 500 ml RPMI = ~ 5 cigarettes/ 10 ml**

FIG. 2A



Whole cell lysate  
Without Immunoprecipitation

FIG. 2B



Whole Cell Lysate  
Immunoprecipitation for Phosphotyrosine

**FIG. 3**

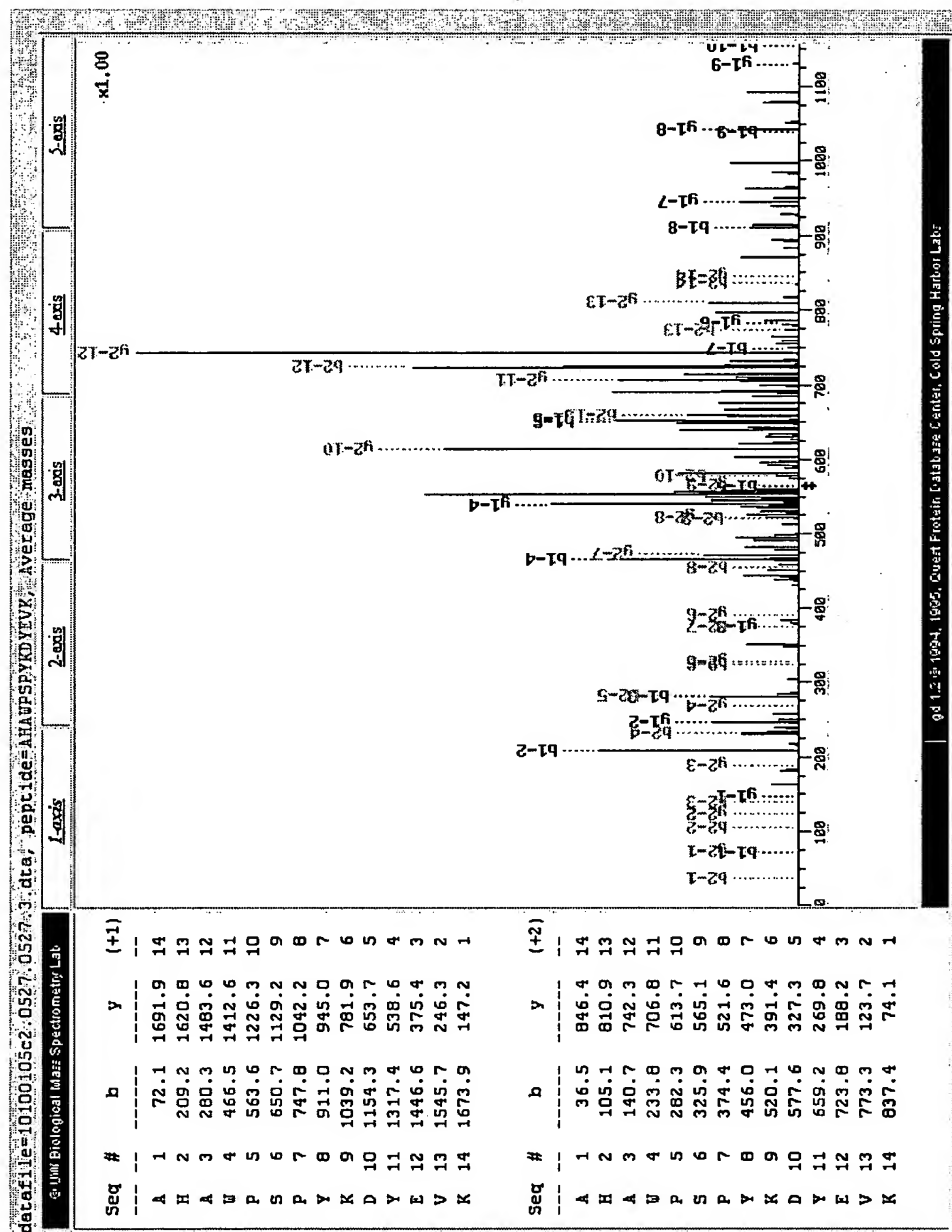


FIG. 4

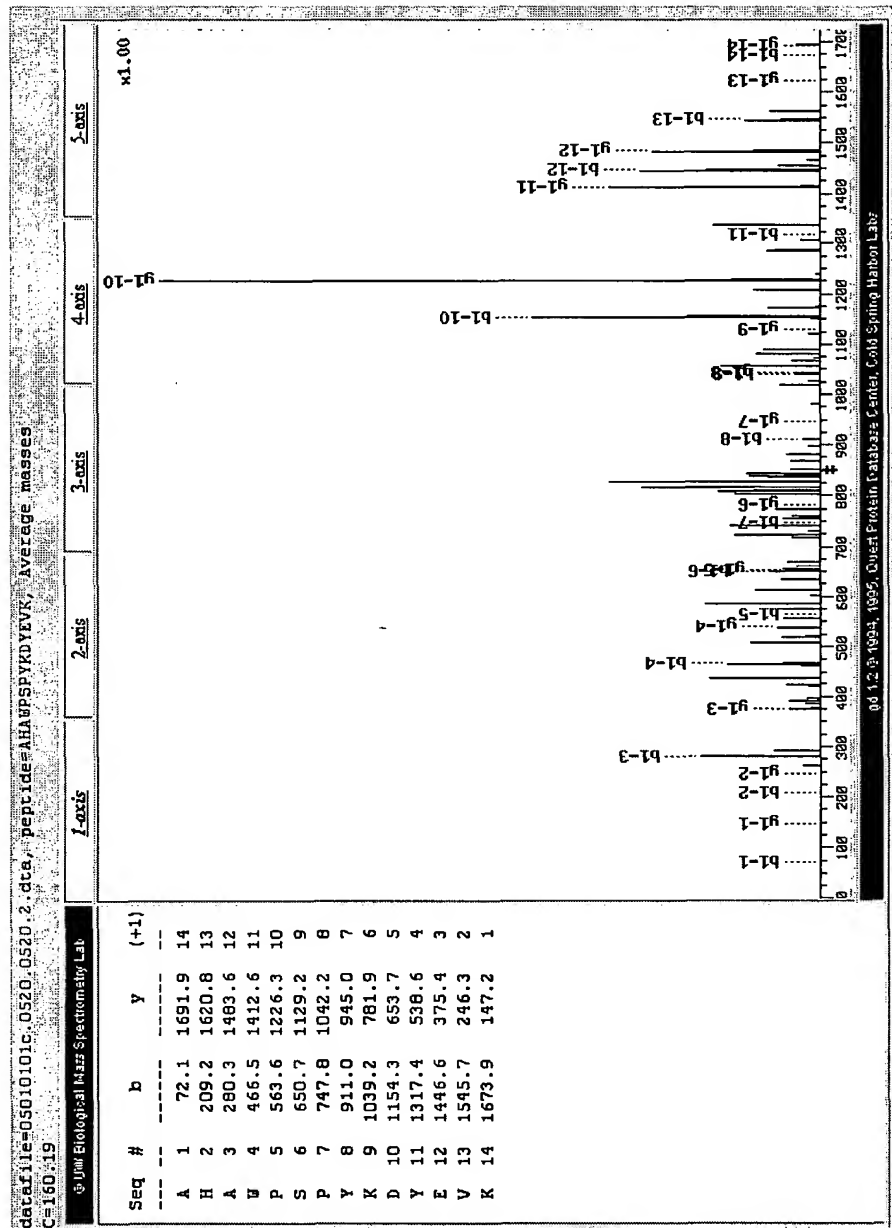


FIG. 5

Treatment of cells with all-trans retinoic acid (ATRA) induces some transcription of RAI-3 mRNA

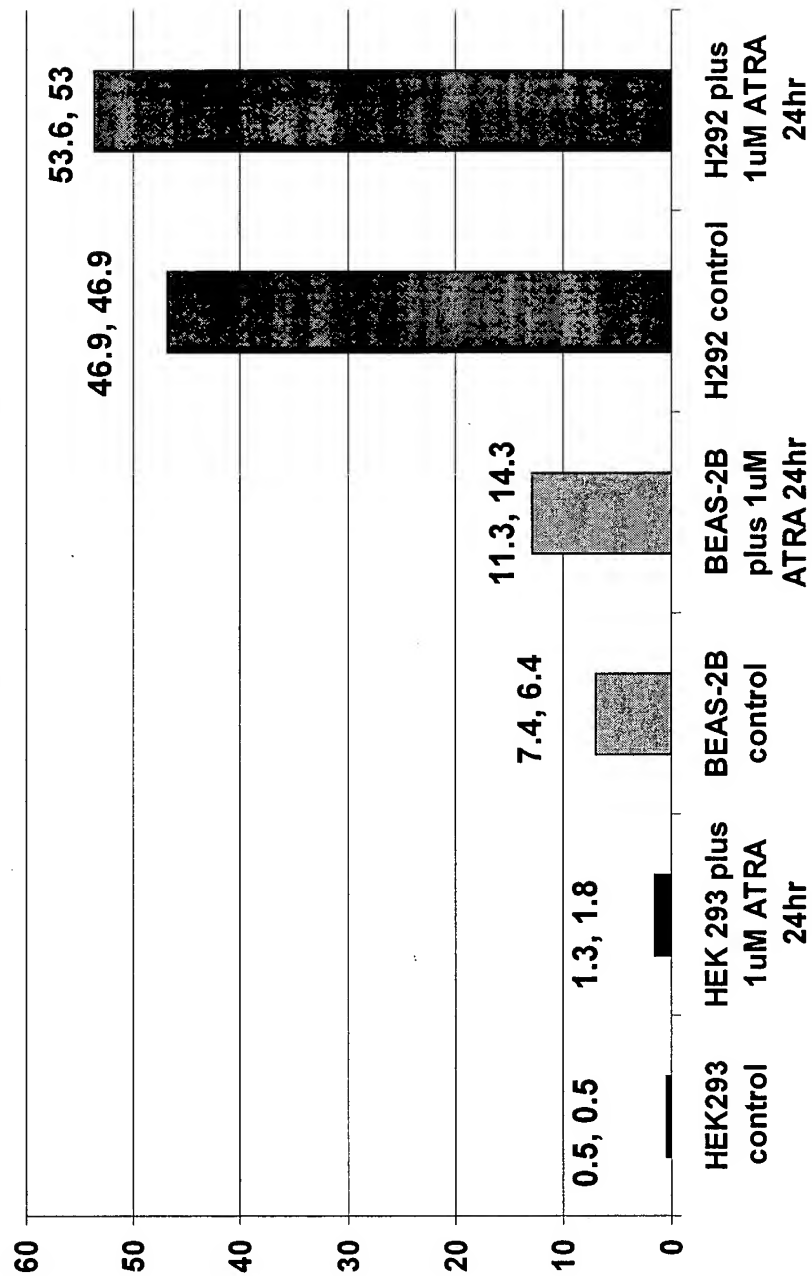


FIG. 6

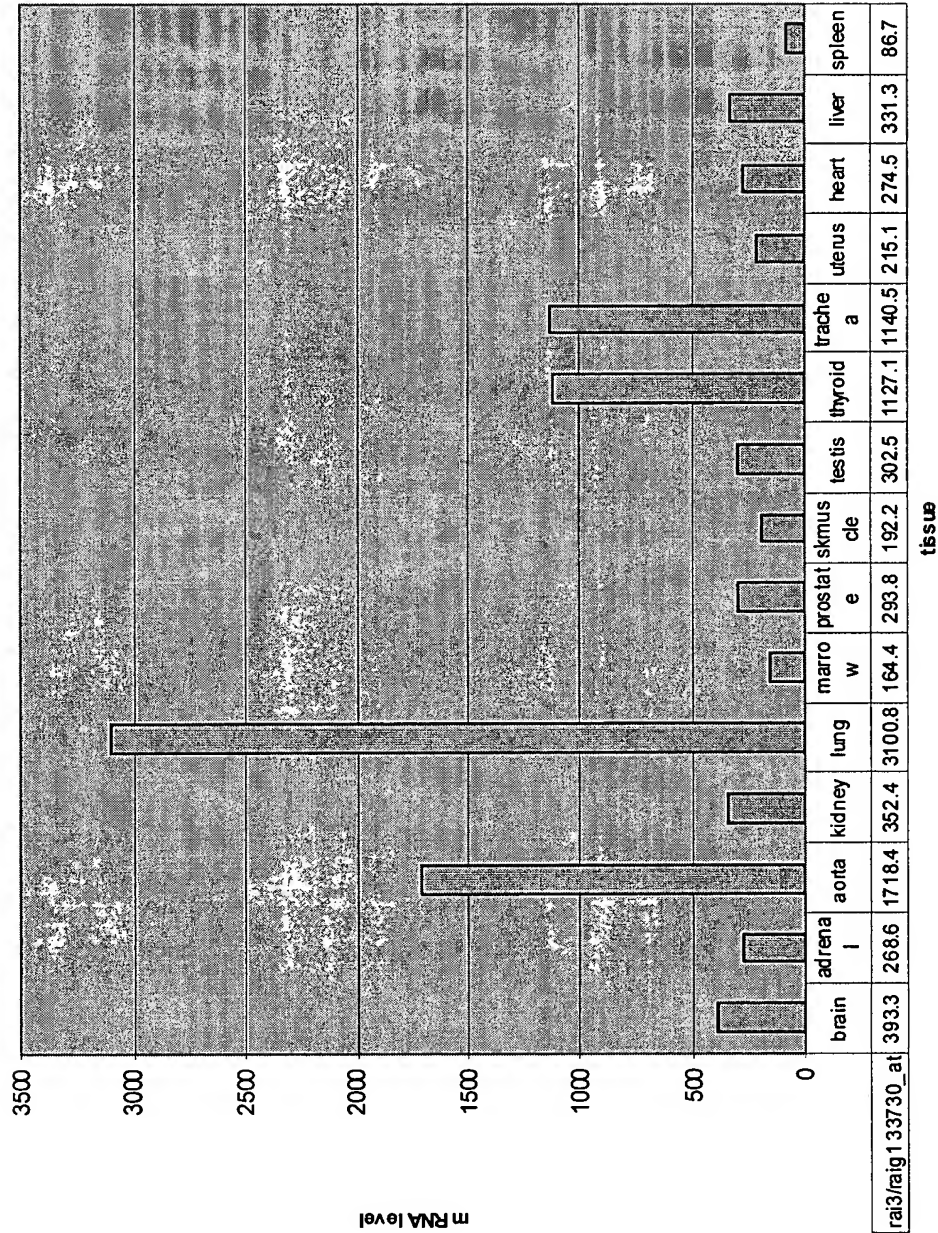


FIG. 7

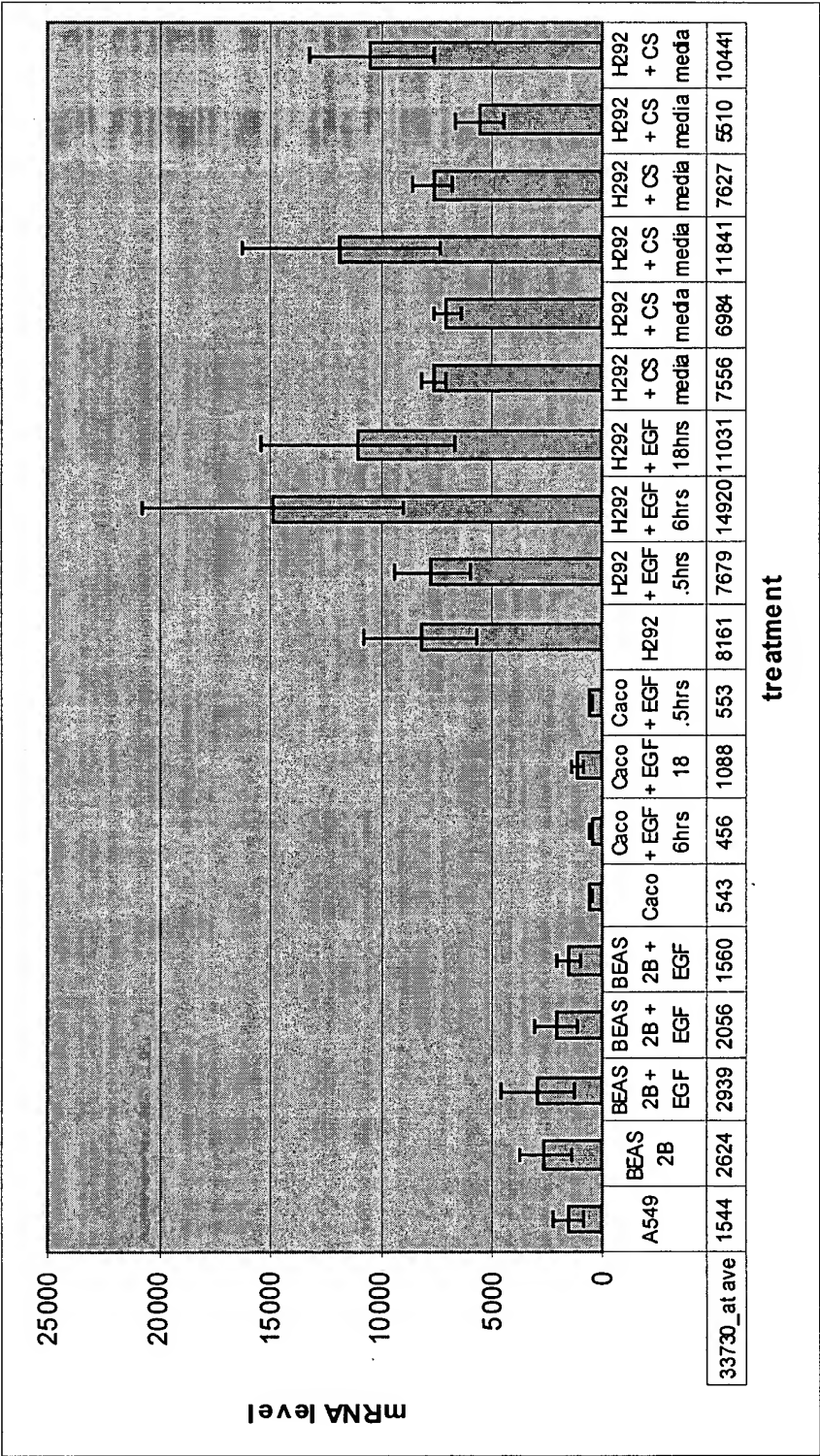
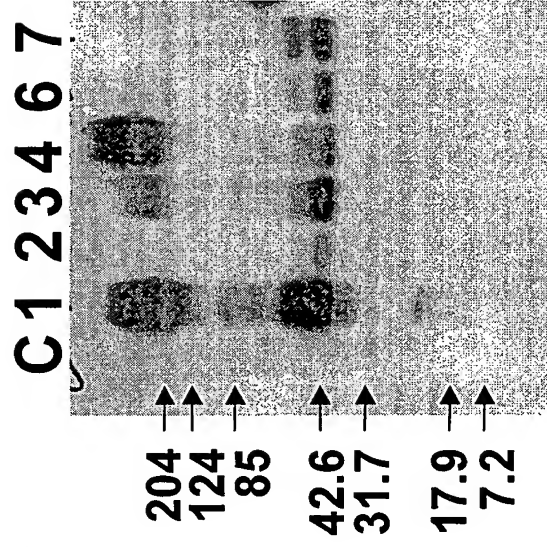
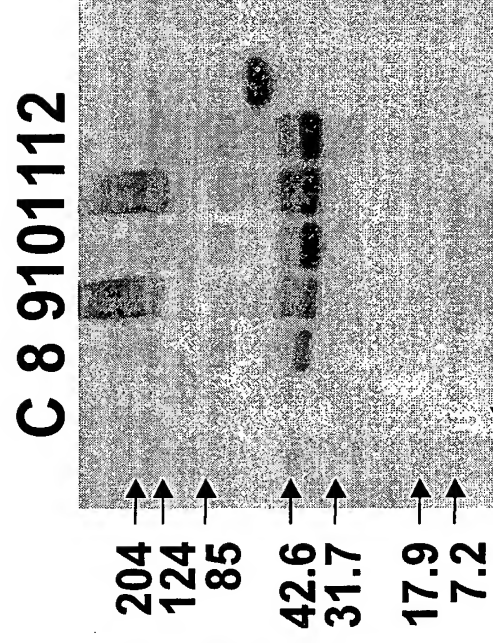


FIG. 8A



Control untransfected  
HEK 293 cells

FIG. 8B



Control FLAG-  
fusion protein  
52/48 kD



FIG. 9A

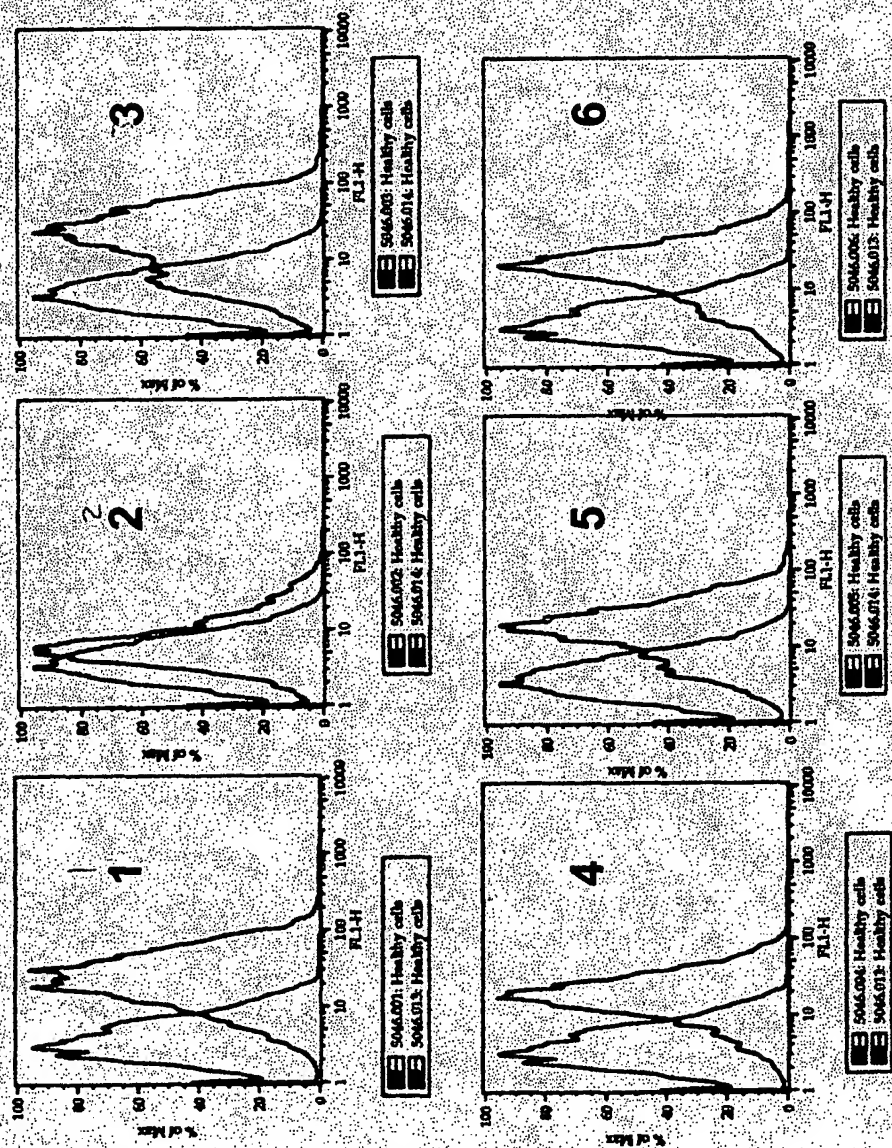


FIG. 9B

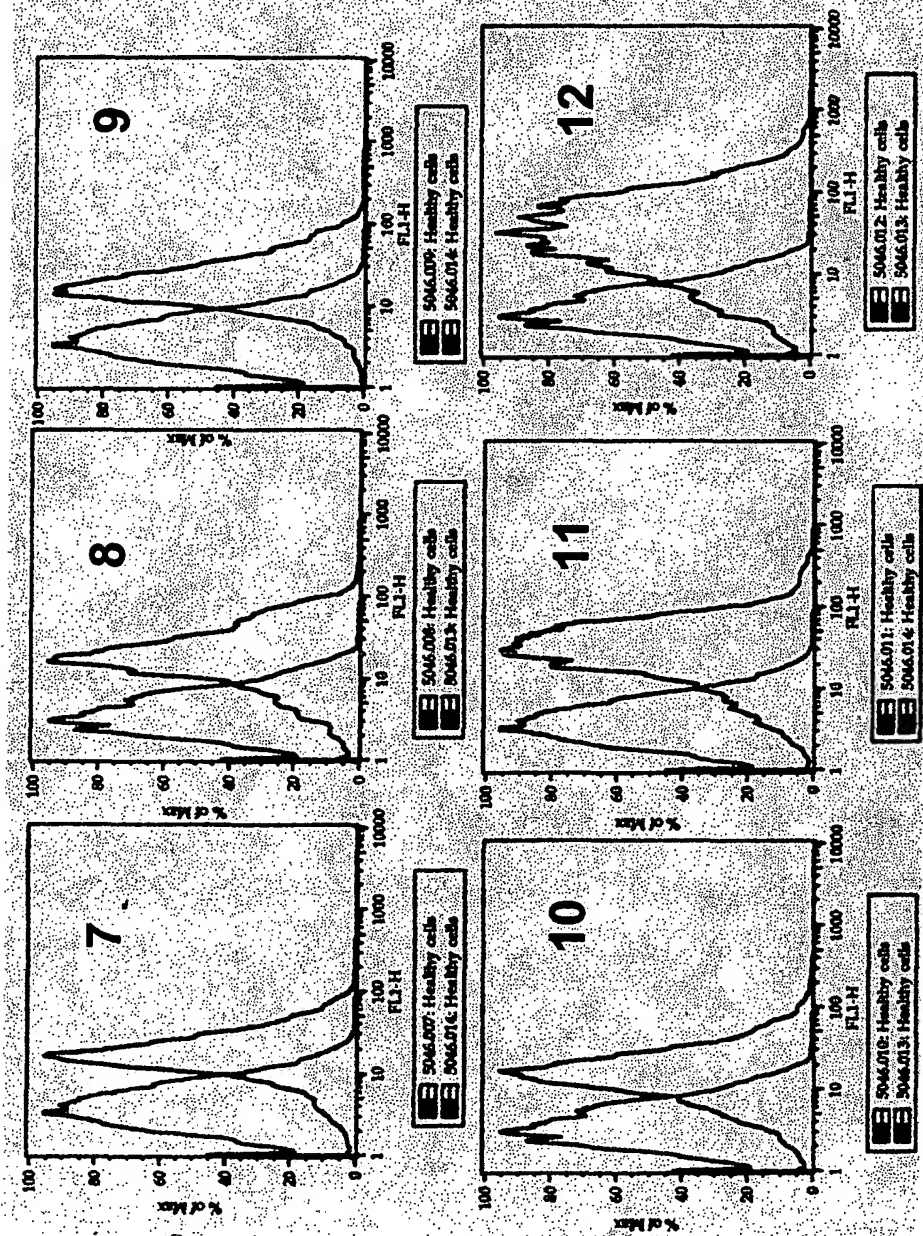


FIG. 10A

1 ataacagcat gaagtgccgt ggaactggaa taggcgtgtc ctctccctcg accctccccc  
61 tccttgctccc tctgctcacc cctcgctcgt tccctccctc cggcgagggc cgcctttata  
121 acaactgctc agagtgcgag ggcgggatag ctgtccaagg tctccccag cactgaggag  
181 ctgcctgct gccctcttgc gcgcgggaag cagcaccaag ttcacggcca acgccttggc  
241 actaggtcc agaatggcta caacagtccc tgatggttgc cgcaatggcc tgaaatccaa  
301 gtactacaga ctttgtgata aggctgaagc ttggggcatc gtcctagaaa cgggtggccac  
361 agccgggggtt gtgacctcgg tggccttcat gtcactctc ccgatcctcg tctgcaaggt  
421 gcaggactcc aacaggcgaa aaatgctgcc tactcagttt ctcttccctc tgggtgtggt  
481 gggcatcttt ggcctcacct tcgccttcat catcgactg gacgggagca cagggcccac  
541 acgcttcttc ctctttggga tctcttttc catctgcttc tctgctgc tggctcatgc  
601 tgtcagtctg accaagctcg tccgggggag gaagcccctt tccctgttgg tgattctggg  
661 tctggccgtg ggcttcagcc tagtccagga tgttatcgt attgaatata ttgtcctgac  
721 catgaatagg accaactca atgtcttttc tgagctttcc gtcctcgtc gcaatgaaga  
781 ctttgtcctc ctgctcacct acgtcctctt cttgatggcg ctgaccttc tcatgtcctc  
841 cttcaccttc tgtggttctt tcacgggctg gaagagacat ggggccaca tctacctcac  
901 gatgctcctc tccattgcca tctgggtggc ctggatcacc ctgctcatgc ttcctgaact  
961 tgaccgcagg tgggatgaca ccctcctcag ctccgccttg gctgccaatg gctgggtgtt  
1021 cctgttggct tatgttagtc ccgagttttg gctgctcaca aagcaacgaa accccatgga  
1081 ttatcctggt gaggatgctt tctgtaaacc tcaactcgtg aagaagagct atggtgtgga  
1141 gaacagagcc tactctcaag aggaaatcac tcaaggtttt gaagagacag gggacacgct  
1201 ctatgcccc tattccacac attttcagct gcagaaccag cctccccaaa aggaattctc  
1261 catcccacgg gccacgctt ggccgagccc ttacaaagac tatgaagtaa agaaagaggg  
1321 cagctaactc tgtcctgaag agtgggacaa atgcagccgg gcggcagatc tagcgggagc  
1381 tcaaagggat gtgggcgaaa tcttgagtct tctgagaaaa ctgtacaaga cactacggga  
1441 acagtttgcc tccctcccag cctcaaccac aattcttcca tgctggggct gatgtgggt  
1501 agtaagactc cagttcttag aggcgctgta gtattttttt ttttttgtct catcctttgg  
1561 atacttcttt taagtgggag tctcaggcaa ctcaagttta gacccttact ctttttggtt  
1621 gttttttgaa acaggatctt gctctgtcac ccaggcttga gtgcagtggg gcgatcacag  
1681 ccagtgacag cctcgaccac ctgtgctcaa gcaatcctcc catctccatc tcccaaagtg  
1741 ctgggatgac aggcgtgagc cacagctccc agcctaggcc cttaatcttg ctgttatctt  
1801 ccatggacta aaggtctggt catctgagct cacgctggct cacacagctc taggggcctg  
1861 ctctctaac tcacagtggg ttttgtgagg ctctgtggcc cagagcagac ctgcatatct  
1921 gagcaaaaat agcaaaagcc tctctcagcc cactggcctg aatctacact ggaagccaac  
1981 ttgctggcac ccccgctccc caacccttct tgctgggta ggagaggcta aagatcacc  
2041 taaatttact catctctcta gtgctgcctc acattgggccc tcagcagctc cccagcacca

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**FIG. 10B**

2101 attcacaggt caccctctc ttcttgact gtccccaac ttgctgtcaa ttccgagatc  
2161 taatctcccc ctacgtctg ccaggaattc tttcagacct cactagcaca agcccggttg  
2221 ctctttgtca ggagaatttg tagatcattc tcacttcaaa ttcctggggc tgatacttct  
2281 ctcatcttgc accccaacct ctgtaaatag atttaccgca tttacggctg cattctgtaa  
2341 gtgggcatgg tctcctaatag gaggagtgtt cattgtataa taagttattc acctgagtat  
2401 gcaataaaga tgtggtggcc actctttcat ggtggtggca gcaaaaaaaaa aaaaaa

**FIG. 11A**

1 MATTVPDGCR NGLKSKYYRL CDKAEAWGIV LETVATAGVV TSVAFMLTLP ILVCKVQDSN  
61 RRKMLPTQFL FLLGVLGIFG LTFAFIIGLD GSTGPTRFFL FGILFSICFS CLLAHAVSLT  
121 KLVGRGRKPLS LLVILGLAVG FSLVQDVIAI EYIVLTMNRT NVNVFSELSA PRRNEDFVLL  
181 LTYVLFLMAL TFLMSSFTFC GSFTGWKRHG AHIYLTMLLS IAIWVAWITL LMLPDFDRRW  
241 DDTILSSALA ANGWFLLAY VSPEFWLLTK QRNPMDYPVE DAFCKPQLVK KSYGVENRAY  
301 SQEETQGF ETDGDTLYAPY STHFQLQNQP PQKEFSIPRA HAWPSPYKDY EVKKEGS

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FIG. 11B

|      |   |      |
|------|---|------|
| 1    | ataacagcatgaagtgccgtggaactggaataggcgtgtcctctccctcgaccctcccc     | 60   |
| 61   | tccttggtccctctgctcaccctcgctcgttcctccctccggcgagggcgccctttata     | 120  |
| 121  | acaactgctcagagtgcgagggcgggatagctgtccaaggtctccccagcactgaggag     | 180  |
| 181  | ctcgctgctgccctcttgcgcgcggaagcagcaccaagttcacggccaacgccttggc      | 240  |
| 241  | actagggtccagaatggctacaacagtcctgatggttgccgcaatggcctgaaatccaa     | 300  |
| 1    | M A T T V P D G C R N G L K S K                                 | 16   |
| 301  | gtactacagactttgtgataaggctgaagcttggggcatcgtcctagaaacgggtggccac   | 360  |
| 17   | Y Y R L C D K A E A W G I V L E T V A T                         | 36   |
| 361  | agccgggggttgtagacctcggtggccttcattgctcactctcccgatcctcgtctgcaaggt | 420  |
| 37   | A G V V T S V A F M L T L P I L V C K V                         | 56   |
| 421  | gcaggactccaacaggcgaaaaatgctgcctactcagtttctcttccctcctgggtgtggt   | 480  |
| 57   | Q D S N R R K M L P T Q F L F L L G V L                         | 76   |
| 481  | gggcattcttggcctcaccttcgccttcattcatcgactggacgggagcacagggccac     | 540  |
| 77   | G I F G L T F A F I I G L D G S T G P T                         | 96   |
| 541  | acgcttcttccctcttgggatcctcttttccattgcttctcctgcctgctggctcatgc     | 600  |
| 97   | R F F L F G I L F S I C F S C L L A H A                         | 116  |
| 601  | tgtcagttctgaccaagctcgtccgggggaggaagccctttccctggttggtgattctggg   | 660  |
| 117  | V S L T K L V R G R K P L S L L V I L G                         | 136  |
| 661  | tctggccgtgggcttcagcctagtccaggatgttatcgctattgaatatattgtcctgac    | 720  |
| 137  | L A V G F S L V Q D V I A I E Y I V L T                         | 156  |
| 721  | catgaataggaccaacgtcaatgtcttttctgagctttccgctcctcgtcgcaatgaaga    | 780  |
| 157  | M N R T N V N V F S E L S A P R R N E D                         | 176  |
| 781  | ctttgtcctcctgctcacctacgtcctcttcttgatggcgctgaccttcctcatgtcctc    | 840  |
| 177  | F V L L L T Y V L F L M A L T F L M S S                         | 196  |
| 841  | cttcaccttctgtggttccttcacgggctggaagagacatggggcccacatctacctcac    | 900  |
| 197  | F T F C G S F T G W K R H G A H I Y L T                         | 216  |
| 901  | gatgctcctctccattgccatctgggtggcctggatcacctgctcatgcttcctgactt     | 960  |
| 217  | M L L S I A I W V A W I T L L M L P D F                         | 236  |
| 961  | tgaccgcaggtgggatgacaccatcctcagctccgccttggctgccaatggctgggtggt    | 1020 |
| 237  | D R R W D D T I L S S A L A A N G W V F                         | 256  |
| 1021 | cctggttgcttatgttagtcccgagttttggctgctcaciaagcaacgaaaccccatgga    | 1080 |
| 257  | L L A Y V S P E F W L L T K Q R N P M D                         | 276  |
| 1081 | ttatcctggttgaggatgctttctgtaaacctcaactcgtgaagaagagctatggtgtgga   | 1140 |
| 277  | Y P V E D A F C K P Q L V K K S Y G V E                         | 296  |
| 1141 | gaacagagcctactctcaagaggaaatcactcaaggttttgaagagacaggggacacgct    | 1200 |
| 297  | N R A Y S Q E E I T Q G F E E T G D T L                         | 316  |

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FIG. 11C

|      |  |      |
|------|--|------|
| 1201 | ctatgccccctattccacacatttttcagctgcagaaccagcctccccaaaaggaattctc  | 1260 |
| 317  | Y A P Y S T H F Q L Q N Q P P Q K E F S                        | 336  |
| 1261 | catcccacgggcccacgcttgccgagcccttacaaagactatgaagtaaagaaagaggg    | 1320 |
| 337  | I P R <u>A H A W P S P Y K D Y E V K</u> K E G                 | 356  |
| 1321 | cagctaactctgtcctgaagagtgggacaaatgcagccgggcggcagatctagcgggagc   | 1380 |
| 357  | S  | 357  |
| 1381 | tcaaagggatgtgggcgaaatcttgagtcttctgagaaaactgtacaagacactacggga   | 1440 |
| 1441 | acagtttgccctccctcccagcctcaaccacaattcttccatgctggggctgatgtgggct  | 1500 |
| 1501 | agtaagactccagttcttagaggcgctgtagtattttttttttgtctcatcctttgg      | 1560 |
| 1561 | atacttcttttaagtgggagctctcaggcaactcaagtttagacccttactctttttgttt  | 1620 |
| 1621 | gttttttgaaacaggatcttgctctgtcaccaggttgagtgcagtgggtgcgatcacag    | 1680 |
| 1681 | cccagtgacgctcgaccacctgtgctcaagcaatcctcccatctccatctcccaaagtg    | 1740 |
| 1741 | ctgggatgacaggcgtgagccacagctcccagcctagggccttaatcttgctgttatttt   | 1800 |
| 1801 | ccatggactaaaggtctggctcatctgagctcacgctggctcacacagctctaggggcctg  | 1860 |
| 1861 | ctcctctaactcacagtgggttttgtgaggctctgtggcccagagcagacctgcatactc   | 1920 |
| 1921 | gagcaaaaatagcaaaagcctctctcagcccactggcctgaatctacactggaagccaac   | 1980 |
| 1981 | ttgctggcacccccgctccccaacccttcttgccctgggtaggagaggctaaagatcaccc  | 2040 |
| 2041 | taaatttactcatctctctagtgtgcctcacattgggcctcagcagctcccagcacca     | 2100 |
| 2101 | attcacaggtcacccctctcttcttgactgtcccaaaacttgctgtcaattccgagatc    | 2160 |
| 2161 | taatctccccctacgctctgccaggaattctttcagacctcactagcacaagcccgggtg   | 2220 |
| 2221 | ctccttgctcaggagaatttgtagatcattctcacttcaaattcctggggctgatacttct  | 2280 |
| 2281 | ctcatcttgacccccaacctctgtaaatagatttaccgcatttacggctgcattctgtaa   | 2340 |
| 2341 | gtgggcatgggtctcctaataggaggagtgttcattgtataataagttattcacctgagtat | 2400 |
| 2401 | gcaataaagatgtggtggccactctttcatggtggtggcagcaaaaaaaaaaaaaa       | 2456 |

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FIG. 12

```

GPCR5D_HUMAN ~~~~~MYKDCIESTGD.YELLCDABGPWGI
GPCR5D_MOUSE ~~~~~MYEDCVKSTED.YYLFCDNEGPAWI
RAI3_HUMAN ~~~~~MATTVPDGCNRGLKSKYYRLCDKAEAWGI
GPCR5B_HUMAN MFVASERKMRAHQVLTFL..LFVITSVASENASTSRGCGLDLLPQYVSLCDLDAIWGI
GPCR5C_HUMAN ~~~~~MAIHKALVMCLGLPLFLFPG.AWAQGHVPPGCSQGLNPLYYNLCDRSGAWGI

GPCR5D_HUMAN TLESLAILGIVVTILLLLAFLFLMRKIQDCSQWNVLPTQLFLLSVLGLFGLAFAFIIEI
GPCR5D_MOUSE VLES LAVIGIVVTILLLLAFLFLMRKVQDCSQWNVLPTQFLFLAVLGLFGLTFAFI IQI
RAI3_HUMAN VLET VATACVVTSAFMLTLPILVCKVQDSNRRKMLPTQFLFLGLVGLTFAFI IGL
GPCR5B_HUMAN VVEAVAGAGATITLLMLLILVRLPFTKEKEKKSPVGLHFLFLGLTGLFGLTFAFI IQE
GPCR5C_HUMAN VLEAVAGAGIVTTFVLTITLVASLPFVQDTKKRSLTGTQVVFLLGTGLGLCLVFACVVKP

GPCR5D_HUMAN NQQTAPVRYFLFGVLFALCFSCLLAHASNVLKLV.R.GCVSFSWTTILCTAIGCSLLOTHI
GPCR5D_MOUSE NHQTAPVRYFLFGVLFALCFSCLLAHASNVLKLV.R.GRVSFCTWTTILFTAGVSLLOTHI
RAI3_HUMAN DGSTGPTREFLEGLTFSICFSCLLAHAVSLTKLV.R.GRKPLSLLVILGLAVGFSLVQDVI
GPCR5B_HUMAN DETICSVRRFLWGVLFALCFSCLLSAWRVRLVRHGTGPAGW.QEVLGALCLMLVQVTHI
GPCR5C_HUMAN DFSTCASRRFLFGVLFALCFSCLLAHVFLNFLARKNHGPRGW.VIFTVAILLTLVEVTHI

GPCR5D_HUMAN ATEYVTLIMTRG.....MMFVNMTPCQL.NVDFVLLVYVFLMALTFF.VSKA
GPCR5D_MOUSE ATEYVTLIMTRG.....LMFEHMTPTYQL.NVDFVCLLIYVFLMALTFF.VSKA
RAI3_HUMAN ATEYIVLTMNRT.....NVNVFSELSAPRR.NEDFVLLIYVFLMALTFF.LMSSF
GPCR5B_HUMAN AVEWLVLTVLR...DTRP.....ACAYEPMDFVMALIYDMVLLV.VTLGLALF
GPCR5C_HUMAN NTEWLLITLVRSGE GGPQGNSSAGWAVASPCA VANMDFVMALIYVMLLLLGAF LG.AWP

GPCR5D_HUMAN TFCGPCENWKQHGRLEFIVLFSIIIWVWISMLLRGNPQFORQPOWDDFVVCIALVTNA
GPCR5D_MOUSE TFCGPCENWKQHGRLEFIVLFSIIIWVWISMLLRGNPQFORQPHWDDAVICIGLVNTA
RAI3_HUMAN TFCGSEITGWKRHGAHIVLTYSIAIWVAWITLLML..PDFDRR..WDDTILSSALAANG
GPCR5B_HUMAN TLCKGKFKRWKLNCAFLITAFISVLIWVAWMTMYLFGNVKLOQGDANDPTLATLAASG
GPCR5C_HUMAN ALCGRYKRWKRGVFLITATSVAIWVWIVMYTYGN.KQHNSETWDDPTLATLAANA

GPCR5D_HUMAN WVFLLLYIVPELCTLYRSCR.QE.....CPLQGNACPVTAHQHSEQ.....VENQELSRA
GPCR5D_MOUSE WVFLLLIYTIPELSILYRSCR.QE.....CPTQGNVCQVPVYQSRER.....MDTQEPITRE
RAI3_HUMAN WVFLLAYVSPEFWLTKQRNPMD.....VPVEDAFCKPOLVKKSYG.....VENRAYSQE
GPCR5B_HUMAN WVVFVIFHAIPET.HCTLLPALQENTPNYEDTSQPRMRETAFEEDVQLPRAYMENKAFSMD
GPCR5C_HUMAN WAFVLFYVVIPEVSQVTKSSPEQSYQDMYPTRGVGY.ETILKEQ.KGQSMFVENKAFSMD

GPCR5D_HUMAN RDSDGAE..DVALTSYGTPIQPQTVDPTQECFIPQAKLSPQDAGGV~~~~~
GPCR5D_MOUSE C~~~~~
RAI3_HUMAN EITQGFEEETGDTLYAPYSTHFQLQNPPQKEFSIPRAHAWPSPYKDYEVKKEGS~~~~~
GPCR5B_HUMAN E.HNAALRTAGFPNGSLGKRPSGLGKRPSAPFRSNVYQPTEMAV..VLNGGTIPTAPP
GPCR5C_HUMAN E.PVAAKRPVS.PY.....SGYNGQ.....LLETSVYQPTEMALMHKVPSE GAYDI ILP

GPCR5D_HUMAN ~~~~~
GPCR5D_MOUSE ~~~~~
RAI3_HUMAN ~~~~~
GPCR5B_HUMAN SHTGRHLW~~~~~
GPCR5C_HUMAN RATANSQVMGSANSTLRAEDMYS AQSHQAATPPKDGKNSQVFRNPYVWD

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FIG. 13

GPCR5D\_HUMAN ~~~~~MYKDCIESTGD.YELLCDAEGPWGI  
 GPCR5D\_MOUSE ~~~~~MYEDCVKSTED.YYLFCDNEGPAI  
 RAI3\_HUMAN ~~~~~MATTVPDGCNRGLKSKYYRLCDKAEAWGI  
 GPCR5B\_HUMAN MFVASERKMRAHQVLTFL...LFVITSVASENASTSRGCGLDLLPQYVSLCDLDAIWGI  
 GPCR5C\_HUMAN ~~~~~MAIHKALVMCLGLPLFLPG.AWAQGHVPPGCSQGLNPLYYNLCDRSGAWGI

GPCR5D\_HUMAN VLESLAILGIVVTLLLLAFLFLMRKIQDCSQWNVLPQTLLFLLSVLGLFGLAFAFIIEE  
 GPCR5D\_MOUSE VLESLAIVIGIVVTLLLLAFLFLMRKVQDCSQWNVLPQTLLFLLAVLGLFGLTFAFIIOE  
 RAI3\_HUMAN VLETVATAGVITSVAFMLTLPILVCKVQDSNRRKMLPTQFLFLLGLVGLIFGLTFAFIIGL  
 GPCR5B\_HUMAN VVEAVAGAGALTLLMLLILLVREPFKEKEKSPVGLHFLFLLGLTGLFGLTFAFIIOE  
 GPCR5C\_HUMAN VLEAVAGAGIVTTFVLTLLILVASLPFVODTKKRSLGTQVFFLLGLTGLFGLTFAFIIOE

GPCR5D\_HUMAN NQQTAPVRYFLFGVLFALCFSCLLAHASNLVKLV...GCVSFSWTTILCTATGCSLLOTH  
 GPCR5D\_MOUSE NHQTAPVRYFLFGVLFALCFSCLLAHASNLVKLV...GRVSFCWTTILCTATGVSLLQTH  
 RAI3\_HUMAN DGSTGPTREFLEGLFSCICFSCLLAHAVSLTKLV...GRKPLSLLVILGLAVGFSLVQDVI  
 GPCR5B\_HUMAN DETICSVRRFLWGVLFALCFSCLLSQAWRVRRRLVRHGTGPAGW.QLVGLALCLMLVQVII  
 GPCR5C\_HUMAN DFSTCASRRFLFGVLFALCFSCLLAHAVFALNFLARKNHGPRGW.VIFTVALLLTLVEVII  
 Variant HUMAN RAI3 G (SNP S/G)

GPCR5D\_HUMAN ATEYVTLIMTRG.....MFEVNMTPCQL.NVDFVLLVYVLFMALTEF.VSKA  
 GPCR5D\_MOUSE ATEYVTLIMTRG.....LMFEHMTPTYQL.NVDFVCLLIYVLFMALTEF.VSKA  
 RAI3\_HUMAN ATEYVTLTMNRT.....NVNVFSELSAPRR.NEDEVLLTYVLFMALTEF.MSSF  
 GPCR5B\_HUMAN AVEWLVTVLR...DTRP.....ACAYEPMDFVMALIYDMVLLV.VTLGLALF  
 GPCR5C\_HUMAN NTEWLLTLTVRSGEGGPQGNSSAGWAVASPCAANMDFVMALIYVMLLLLGAFGLG.AWP

GPCR5D\_HUMAN TFCGPCENWKQHGRLIFITVLFSTIIWVVWISMLLRGNPQFQRPQWDDDEVVCIALVTNA  
 GPCR5D\_MOUSE TFCGPCENWKQHGRLIFATVLVSIIIWVVWISMLLRGNPQLQRQPHWDDAVICIGLVTNA  
 RAI3\_HUMAN TFCGSETGWKRHGAHIYLTMLLSIAIWWAVITLLML..PDFDR..WDDTILSSALAANG  
 GPCR5B\_HUMAN TLCKGKRWKLNCAFLITAFLSVLIWVAMTMYLFGNVKLOQGDANDPTLATLAASG  
 GPCR5C\_HUMAN ALCGRMKRWKRGVFLITATSVAIWVVWIVMYTYGN.KOHNSPTWDDPTLATALAANA

GPCR5D\_HUMAN WVFLLYVPELCILYRSCR.QE.....CFLOGNACPVTAYQHSEQ.....VENQELSRA  
 GPCR5D\_MOUSE WVFLLYIYIPELSILYRSCR.QE.....CPTQGNVCQVPVYQSRER.....MDTQEPTRF  
 RAI3\_HUMAN WVFLLAYVSPEFWLLTKQRNPMD.....YFVEDAFCKPQLVKKSYG.....VENRAYSOE  
 GPCR5B\_HUMAN WVEVTFHAIPEI.HCTLLPALQENTPNYEDTSQPRMRETAFEEDVQLPRAYMENKAESMD  
 GPCR5C\_HUMAN WAEVLFYVPEVSQVTKSSPEQSYQGDMPYTRGVGY.ETILKEQ.KGQSMFVENKAESMD

GPCR5D\_HUMAN RDSDCAE..DVALTSYGTPIQPQTVDPTQECFIPQAKLSPOQDAGGV~~~~~  
 GPCR5D\_MOUSE C~~~~~  
 RAI3\_HUMAN EITQGFEEETGDTLYAPYSTHFQLQNPPQKEFSTIPRAHAWPSPYKDYEYKKEGS~~~~~  
 GPCR5B\_HUMAN E.HNAALRTAGFPNGSLGKRPSGSLGKRPSAPFRSNVYQPTEMAV...VLNGGTIPTAPP  
 GPCR5C\_HUMAN E.PVAAKRPVS.PY.....SGYNGQ.....LLTSVYQPTMALMHKVPSEGAYDIILP  
 Variant HUMAN R (SNP Q/R)  
 RAI3

GPCR5D\_HUMAN ~~~~~  
 GPCR5D\_MOUSE ~~~~~  
 RAI3\_HUMAN ~~~~~  
 GPCR5B\_HUMAN SHTGRHLW~~~~~  
 GPCR5C\_HUMAN RATANSQVMGSANSTLRAEDMYSAQSHQAATPPKDGKNSQVFRNPYVWD

FIG. 14A

**Antisense to RAI3 Increased Expression of IκB mRNA in A549 Cells**

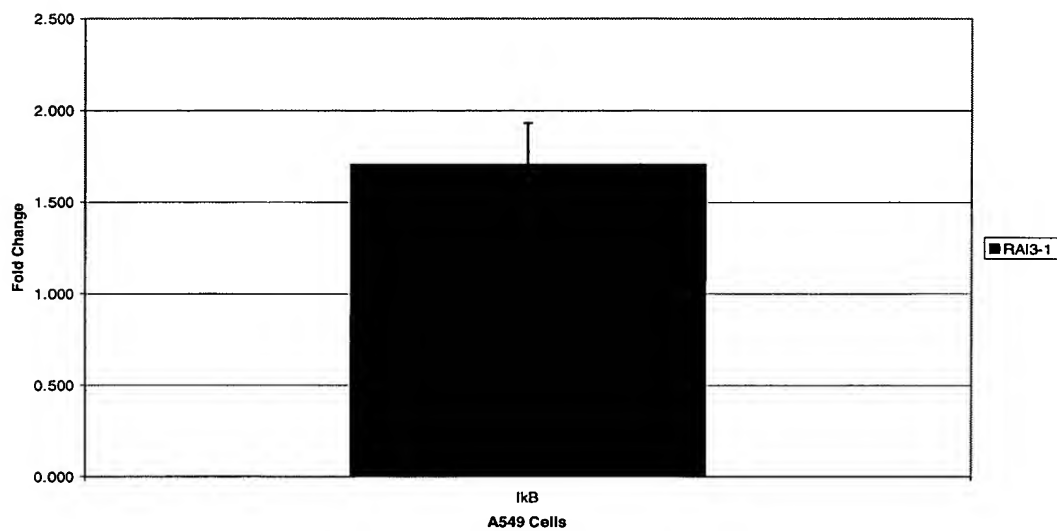
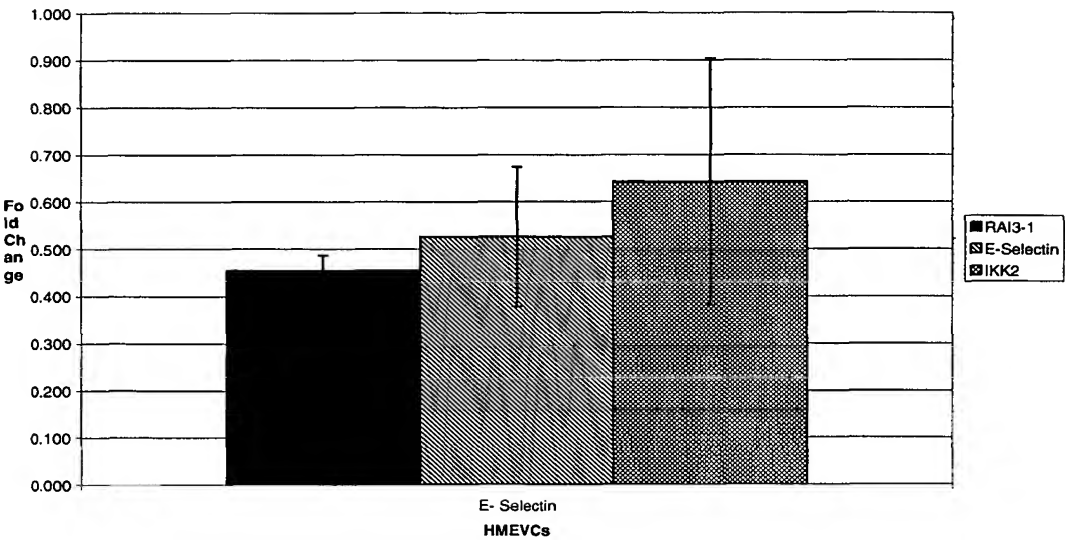


FIG. 14B

Antisense to RAI3 Reduced Expression of E-Selectin on HMEVC's



RAI-3 Relative Expression in normal Tissue RNAs

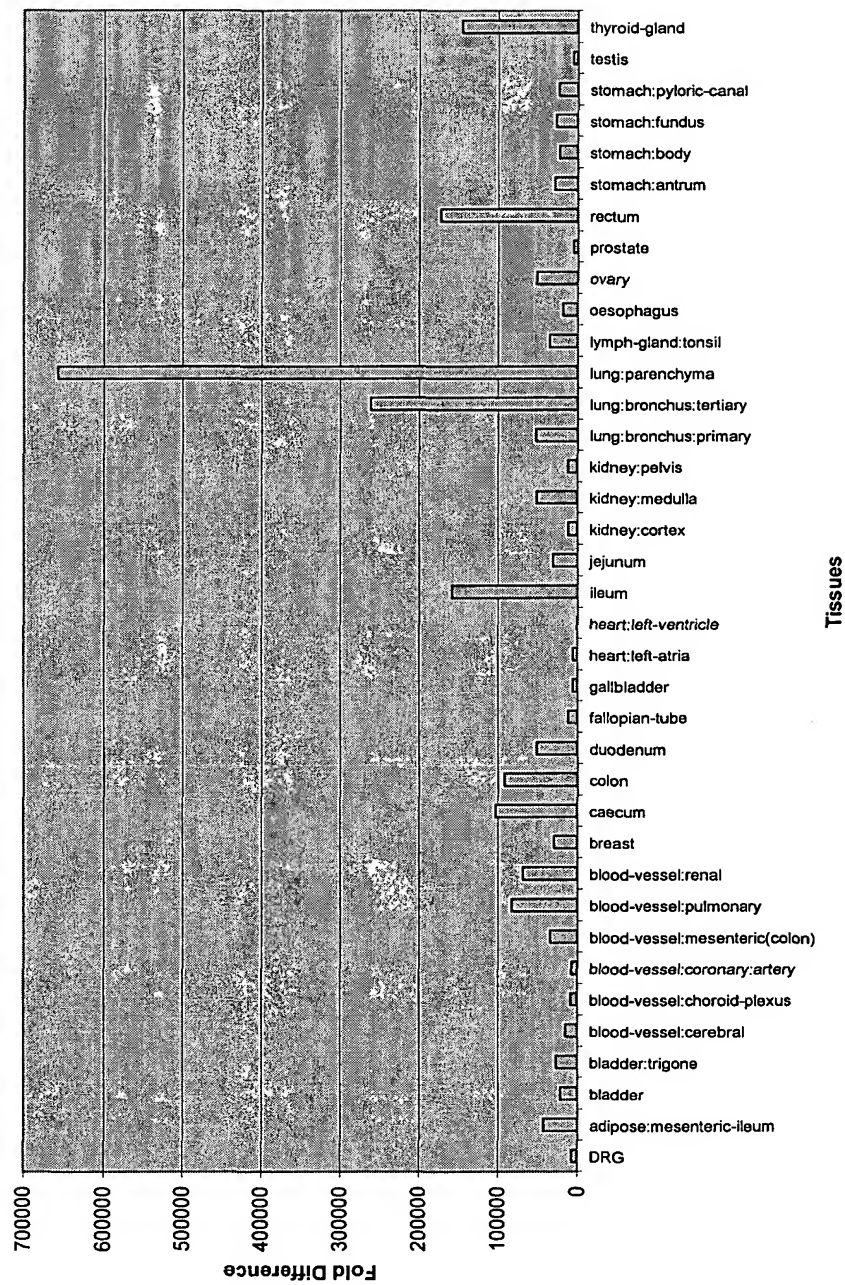


FIG. 16

## RAI3 Relative Expression in Control and Breast Tumors

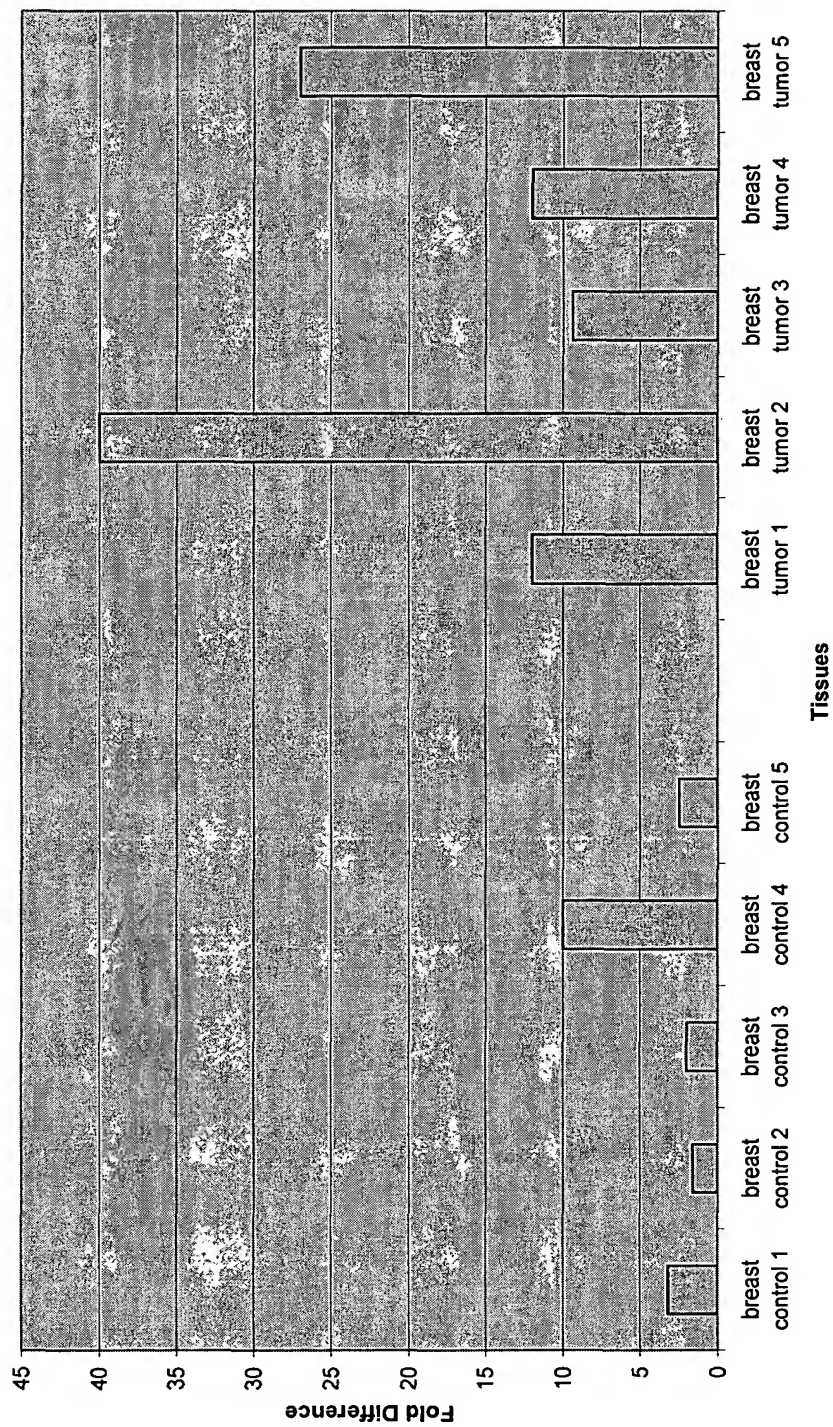


FIG. 17

## RAI3 Relative Expression in Control and Stomach Tumors

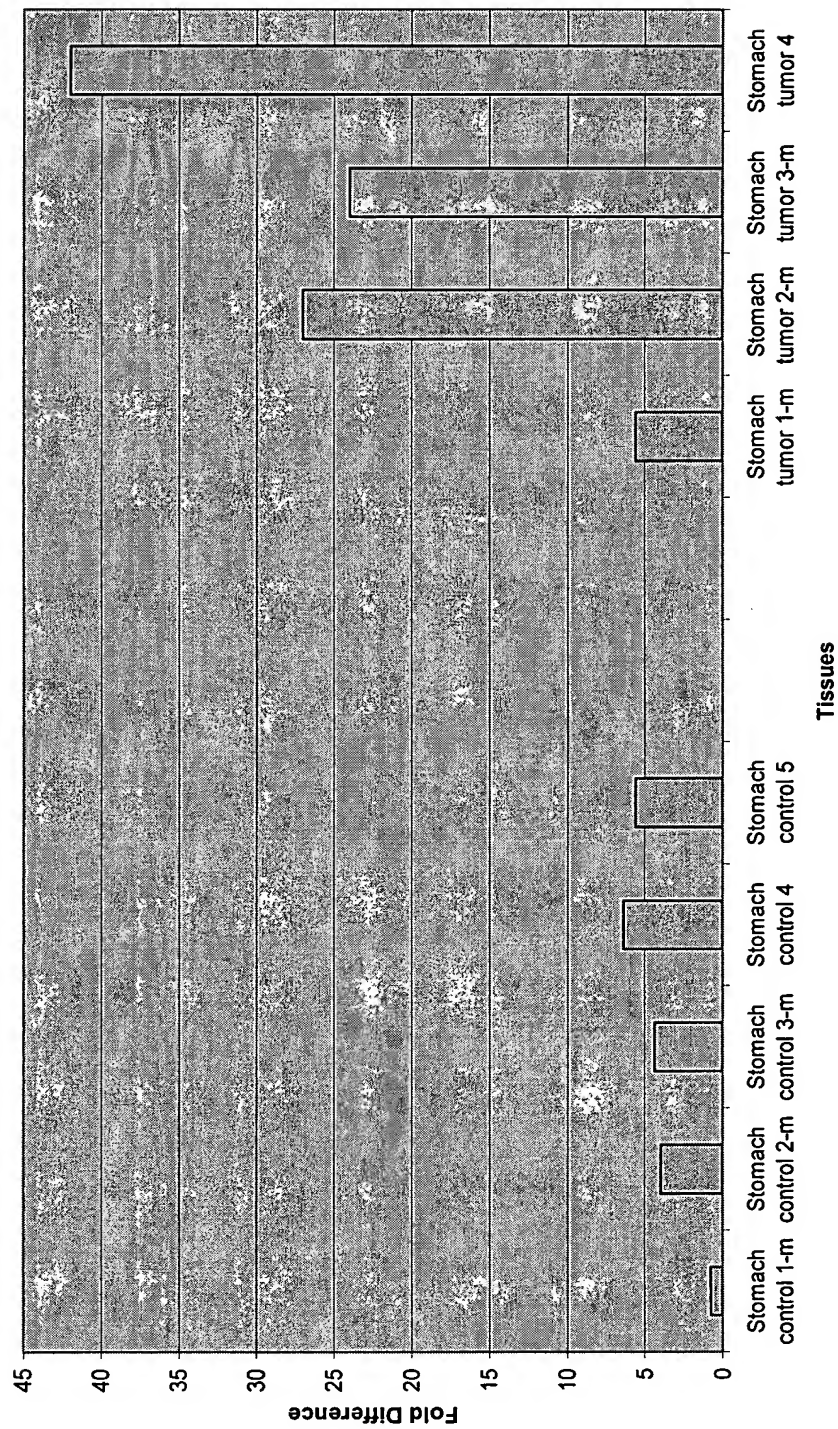




FIG. 18

RAI3 Relative Expression in Control and Testis Tumors

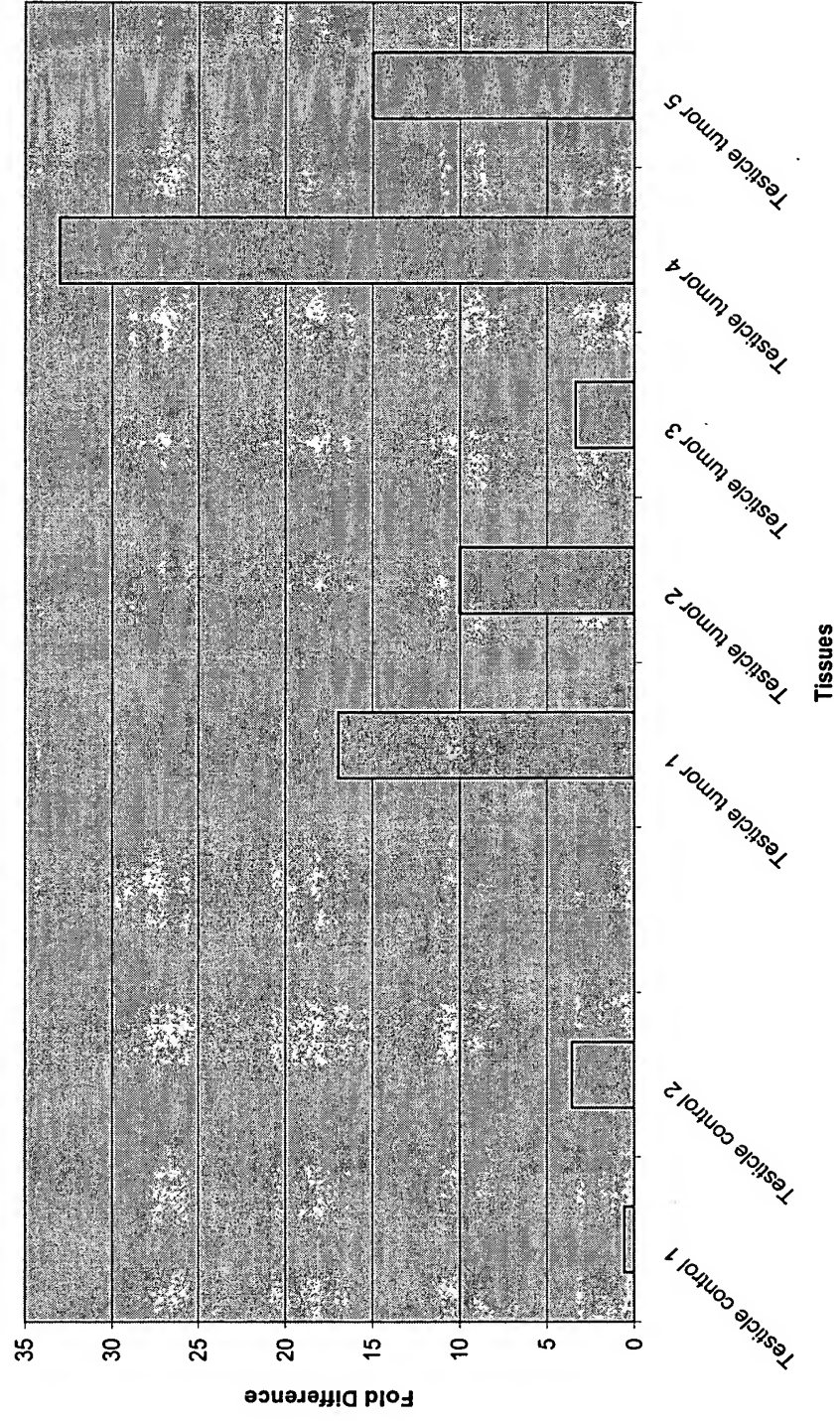


FIG. 19A

GPCR5D\_HUMAN NQQTAPVRYFLEFGLFALCFSCLLAHASNLVKLVRGCVSFSWTTILCIAIGCSLLQIII  
 GPCR5D\_MOUSE NHQTAPVRYFLEFGLFAICFSCLLAHASNLVKLVRGRVVSFCWTTILFIAIGVSLLQTII  
 RAI3\_HUMAN DGSTGPTREFFLEFGLFSICFSCLLAHAVSLTCLVRGRKPLSLLVILGLAVGFSLVQDVI  
 RAI3\_MOUSE DGATGPTREFFLEFGLFAICFSCLLAHAFNLKLVGRGRKPLSWLVILSLAVGFSLVQDVI  
 RAI3\_RAT DRATGPTREFFLEFGLFALCFSCLLAHAFNLKLVGRGRKPLSWLVILSLAVGFSLVQDVI  
 RAI3\_COW NGGTGPTREFFLEFGLFALCFSCLLVHAFNLTKLVGRGRQPLSMLVMLGLALGFSLVQDII  
 RAI3\_HUMAN DGSTGPTREFFLEFGLFSICFSCLLAHAVGLTCLVRGRKPLSLLVILGLAVGFSLVQDVI  
 (w/SNP S/G)

FIG. 19B

GPCR5D\_HUMAN RDSDGAE..DVALTSYGTPIQPQTVDPQTQECFIPQAKLSPQQDAGGV~~~~~  
 GPCR5D\_MOUSE C~~~~~  
 RAI3\_HUMAN EITQGFEETGDTLYAPYSTHFQLQNQPQKEFSIPRAHAWPSPYKDYEYKKEGS~~~~~  
 RAI3\_MOUSE EITQGL.EMGDTLYAPYSTHFQLQNH..QKDFSIPRAQAPASPYNDYEGRKGDS  
 RAI3\_HUMAN EITRGFEETGDTLYAPYSTHFQLQNQPQKEFSIPRAHAWPSPYKDYEYKKEGS~~~~~  
 (w/SNP Q/R)



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FIG. 20

HUMAN: 6 PDGCRNGLKSKYYRLCDKAEAWGIVLETVATAGVVTSVAFMLTLPILVCKVQDSNRRKML 65  
 P GCR+ L S+Y+RLCD AE WGI LET A G V VA M L L+CKVQDSN+RKML  
 MOUSE: 124 PSGCRSDLDSRYHRLCDLAEGWGIALETAAVGAVATVACMFALVFLICKVQDSNKRKML 303

HUMAN: 66 PTQFLFLLGVLGIFGLTFAFIIGLDGSTGPTRFFLFGILFSICFSCLLAHAVSLTKLVRG 125  
 P QFLFLLGVLG+FGLTFAFII LDG+TGPTRFFLFG+LF+ICFSCLLAHA +L KLV RG  
 MOUSE: 304 PAQFLFLLGVLGVFGLTFAFI IKLDGATGPTRFFLFGVLFAICFSCLLAHAFNLIKLV RG 483

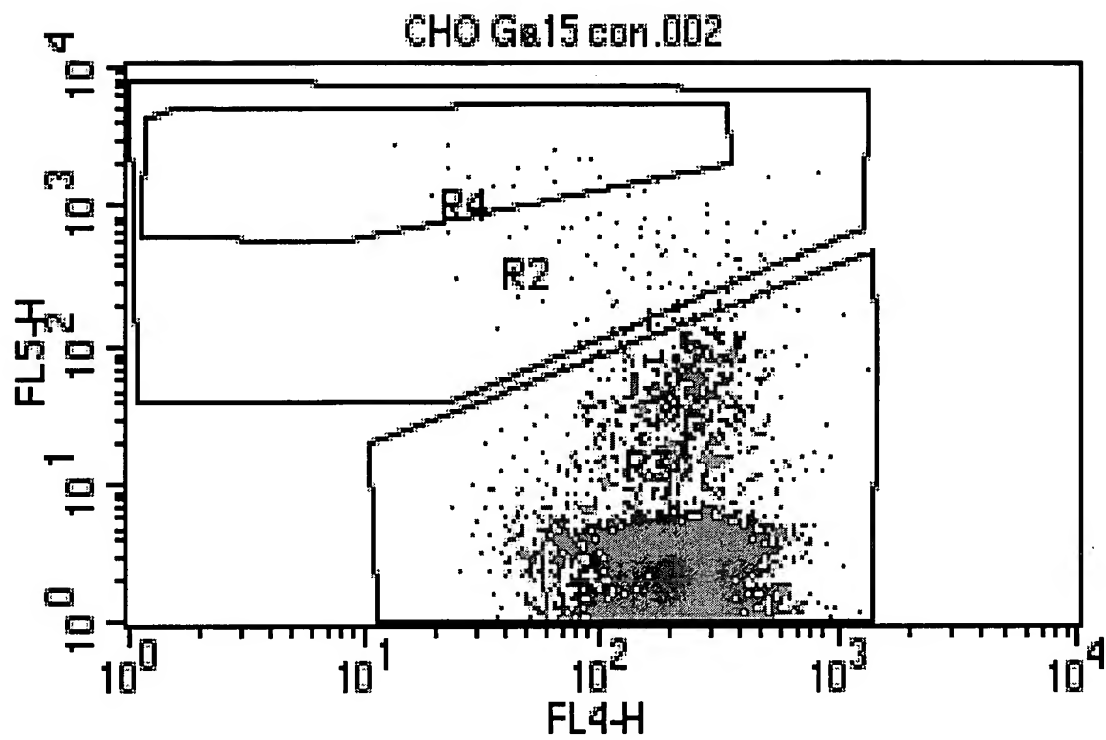
HUMAN: 126 RKPLSLLVILGLAVGFSLVQDVIAIEYIVLTMNRTNVNVFSELSAPRRNEDFVLLLYVL 185  
 RKPLS LVIL LAVGFSLVQDVIAIEY+VLTMNRTNVNVFSEL APRRNEDFV+LL YVL  
 MOUSE: 484 RKPLSWLVILSLAVGFSLVQDVIAIEYLVLTMNRTNVNVFSELPAPRRNEDFVMLLIYVL 663

HUMAN: 186 FLMALTFMLSSFTFCGSFTGWKRHG AHIYLTMLLSIAIWVAWITLLMLPDFDRRWDDTIL 245  
 LM LTF S FCGSF+GWKRHG HI T LSIWVAWI LL++PD DR+WDDTIL  
 MOUSE: 664 VLMVLTFFASFLVFCGSFSGWKRHGFHICFTSFLSIWVAWIVLLLIPDIDRKWDDTIL 843

HUMAN: 246 SSALAANGWVFLLAYVSPEFWLLTKQRNPM DYPVEDAFCKPQLVKKSYGVENRAYSQEEI 305  
 S+AL ANGWVFL Y+ PEF L +QR+P DYPVEDAFCKPQL+K+SYGVENRAYSQEEI  
 MOUSE: 844 STALVANGWVFLAFYILPEFRQLPRQRSPTDYPVEDAFCKPQLMKQSYGVENRAYSQEEI 1023

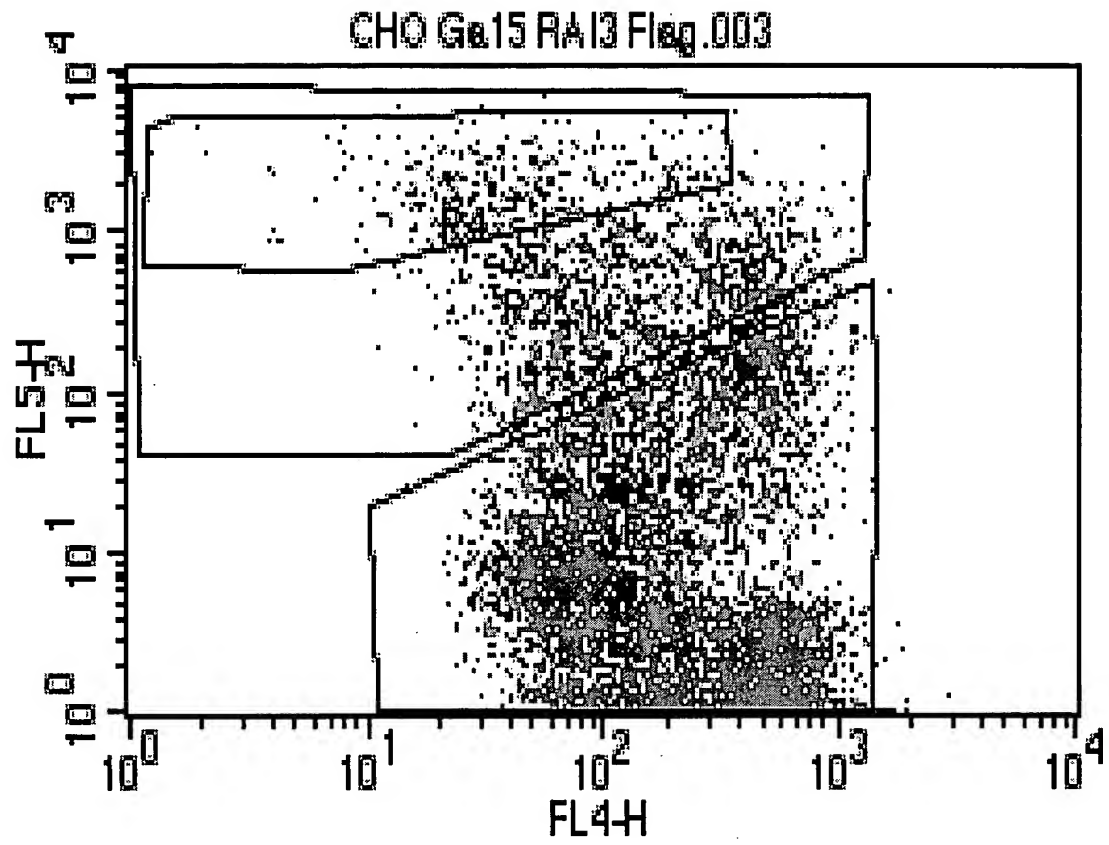
HUMAN: 306 TQGFEETGDTLYAPYSTHFQLQNQPPQKEFSIPRAHAWPSPYKDYE VKKEGS 357  
 TQG E GDTLYAPYSTHFQLQN QK+FSIPRA A SPY DYE +K S  
 MOUSE: 1024TQGL-EMGDTLYAPYSTHFQLQNH--QKDFSIPRAQAPASPYNDYEGRKGDS 1170

FIG. 21



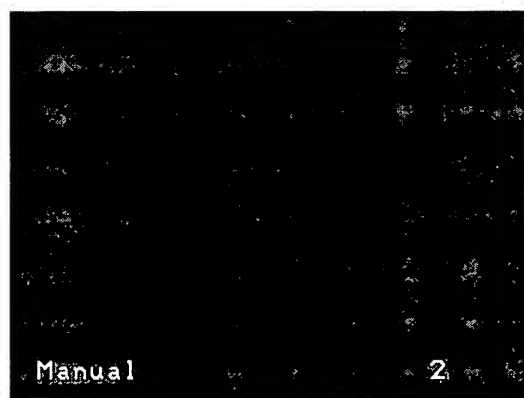
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FIG. 22



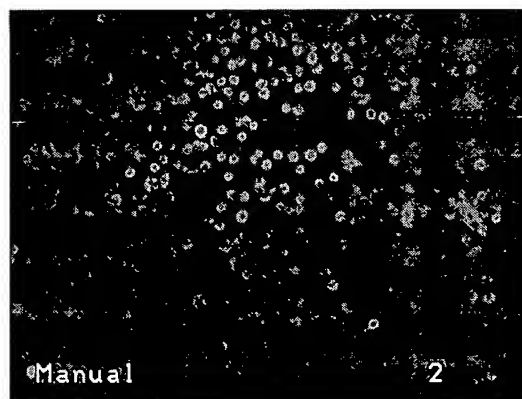
**FIG. 23A**

CHO NFAT Ga15 Control (Fluorescence)



**FIG. 23B**

CHO NFAT Ga15 RAI-3 (Fluorescence)



**FIG. 24A**

**CHO NFAT Ga15**



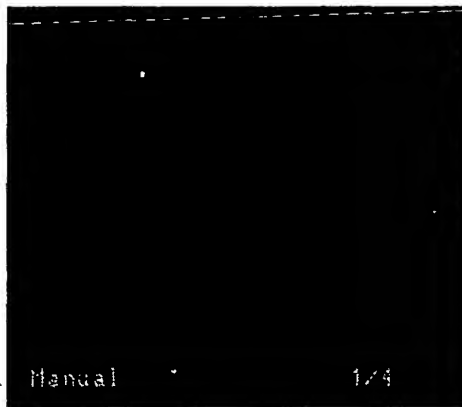
**FIG. 24B**

**CHO NFAT Ga15 + T/P**



**FIG. 24C**

**CHO NFAT Ga15 oGPCR  
Intermediate**



**FIG. 24D**

**CHO NFAT Ga15 oGPCR  
High**



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FIG. 25A

|     |   |     |
|-----|---|-----|
| 1   | ataacagcatgaagtgccgtggaactggaataggcgtgtcctctccctcgaccctccccc  | 60  |
| 61  | tccttgtccctctgctcaccctcgctcggtccctccctccggcgagggccncctttata   | 120 |
| 121 | acaactgctcagagtgcgagggcgggatagctgtccaaggtctccccagcactgaggag   | 180 |
| 181 | ctcgctgctgccctcttgcgcgcggaagcagcaccaagttcacggccaacgccttggc    | 240 |
| 241 | actagggtccagaatggctacaacagtcctgatggttgccgcaatggcctgaaatccaa   | 300 |
| 1   | M A T T V P D G C R N G L K S K                               | 16  |
| 301 | gtactacagactttgtgataaggctgaagcttggggcatcgtcctagaaacgggtggccac | 360 |
| 17  | Y Y R L C D K A E A W G I V L E T V A T                       | 36  |
| 361 | agcnggggttgtagacctcggtggccttcattgctcactctcccgatcctcgctgcaaggt | 420 |
| 37  | A G V V T S V A F M L T L P I L V C K V                       | 56  |
| 421 | gcaggactccaacaggcgaaaaatgctgcctactcagtttctcttcctcctgggtgtgtt  | 480 |
| 57  | Q D S N R R K M L P T Q F L F L L G V L                       | 76  |
| 481 | gggcatccttggcctcaccttcgccttcattatcggaactggangggagcacagggcccac | 540 |
| 77  | G I F G L T F A F I I G L D G S T G P T                       | 96  |
| 541 | acgcttcttcctctttgggatcctcttttccattctgcttctcctgcctgctggctcatgc | 600 |
| 97  | R F F L F G I L F S I C F S C L L A H A                       | 116 |
| 601 | tgtcngtctgaccaagctcgtcggggggaggaagcccctttccctggttggtgattctggg | 660 |
| 117 | V X L T K L V R G R K P L S L L V I L G                       | 136 |
| 661 | tctggccgtgggcttcagcctagtcaggatgttatcgctattgaatatattgtcctgac   | 720 |
| 137 | L A V G F S L V Q D V I A I E Y I V L T                       | 156 |
| 721 | catgaataggaccaacgtcaatgtcttttctgagctttccgctcctcgctgcaatgaaga  | 780 |
| 157 | M N R T N V N V F S E L S A P R R N E D                       | 176 |
| 781 | ctttgtcctcctgctcncctacgtcctcttcttgatggcgctgaccttcctcatgtcctc  | 840 |
| 177 | F V L L L X Y V L F L M A L T F L M S S                       | 196 |

FIG. 25B

|      |  |      |
|------|--|------|
| 841  | cttcaccttctgtggttccttcacgggctggaagagacatggggccacatctacctcac  | 900  |
| 197  | F T F C G S F T G W K R H G A H I Y L T                      | 216  |
| 901  | gatgctcctctccattgccatctgggtggcctggatcaccctgctcatgcttctgactt  | 960  |
| 217  | M L L S I A I W V A W I T L L M L P D F                      | 236  |
| 961  | tgaccgcaggtgggatgacaccatcctcagctccgccttggtgccaatggctgggtggt  | 1020 |
| 237  | D R R W D D T I L S S A L A A N G W V F                      | 256  |
| 1021 | cctggttggttatgttagtcccaggttttggtgctcacaagcaacgaaaccccatgga   | 1080 |
| 257  | L L A Y V S P E F W L L T K Q R N P M D                      | 276  |
| 1081 | ttatcctgttgaggatgctttctgtaaaccncaactcgtgaagaagagctatggtgtgga | 1140 |
| 277  | Y P V E D A F C K P Q L V K K S Y G V E                      | 296  |
| 1141 | gaacagagcctactctcaagaggaaatcactcnaggttttgagagacaggggacacgct  | 1200 |
| 297  | N R A Y S Q E E I T X G F E E T G D T L                      | 316  |
| 1201 | ctatgccccctattccacacattttcagctgcagaaccagcctccccaaaaggaattctc | 1260 |
| 317  | Y A P Y S T H F Q L Q N Q P P Q K E F S                      | 336  |
| 1261 | catcccacgggcccacgcttgccgagcccttacaaagactatgaagtaaagaaagaggg  | 1320 |
| 337  | I P R <u>A H A W P S P Y K D Y E V K</u> K E G               | 356  |
| 1321 | cagctaactctgtcctgaagagtgggacaaatgcagccgggaggagatctagcgggagc  | 1380 |
| 357  | S  | 357  |
| 1381 | tcaaagggatgtgggcgaaatcttgagtcttctgagaaaactgtacaagacactacggga | 1440 |
| 1441 | acagtttgcctccctcccagcctcaaccacaattcttccatgctggggctgatgtgggct | 1500 |
| 1501 | agtaagactccagttcttagaggcgctgtagtattttttttttgtctcatcctttgg    | 1560 |
| 1561 | atacttcttttaagtgggagtctcaggcaactcaagtttagacccttactctttttgttt | 1620 |
| 1621 | gttttttgaaacaggatcttgctctgtcaccagcgttgagtgcagtgggtgcgatcacag | 1680 |

FIG. 25C

1681   cccagtgcagcctcgaccacctgtgctcaagcaatcctcccattctccatctcccaaagtg   1740  
1741   ctgggatgacaggcgtgagccacagctcccagcctaggcccttaatcttgctgttatttt   1800  
1801   ccatggactaaaggtctggtcatctgagctcacgctggctcacacagctctaggggcctg   1860  
1861   ctcctctaactcacagtgggttttgtgaggctctgtggcccagagcagacctgcatatct   1920  
1921   gagcaaaaatagcaaaagcctctctcagcccactggcctgaatctacactggaagccaac   1980  
1981   ttgctggcacccccgctccccaacccttcttgctgggtaggagaggctaaagatcaccc   2040  
2041   taaatttactcatctctctagtgtgcctcacattgggcctcagcagctccccagcacca   2100  
2101   attcacaggtcacccctctcttcttgcaactgtcccaaaacttgctgtcaattccgagatc   2160  
2161   taatctccccctacgctctgccaggaattctttcagacctcactagcacaaagcccggttg   2220  
2221   ctccttgctcaggagaattttagatcattctcacttcaaattcctggggctgatacttct   2280  
2281   ctcatcttgaccccaacctctgtaaatagatttaccgcatttacggctgcattctgtaa   2340  
2341   gtgggcatggtctcctaattggaggagtgttcattgtataataagttattcacctgagtat   2400  
2401   gcaataaagatgtggtggcactctttcatggtggtggcagcaaaaaaaaaaaaaa   2456



FIG. 26A

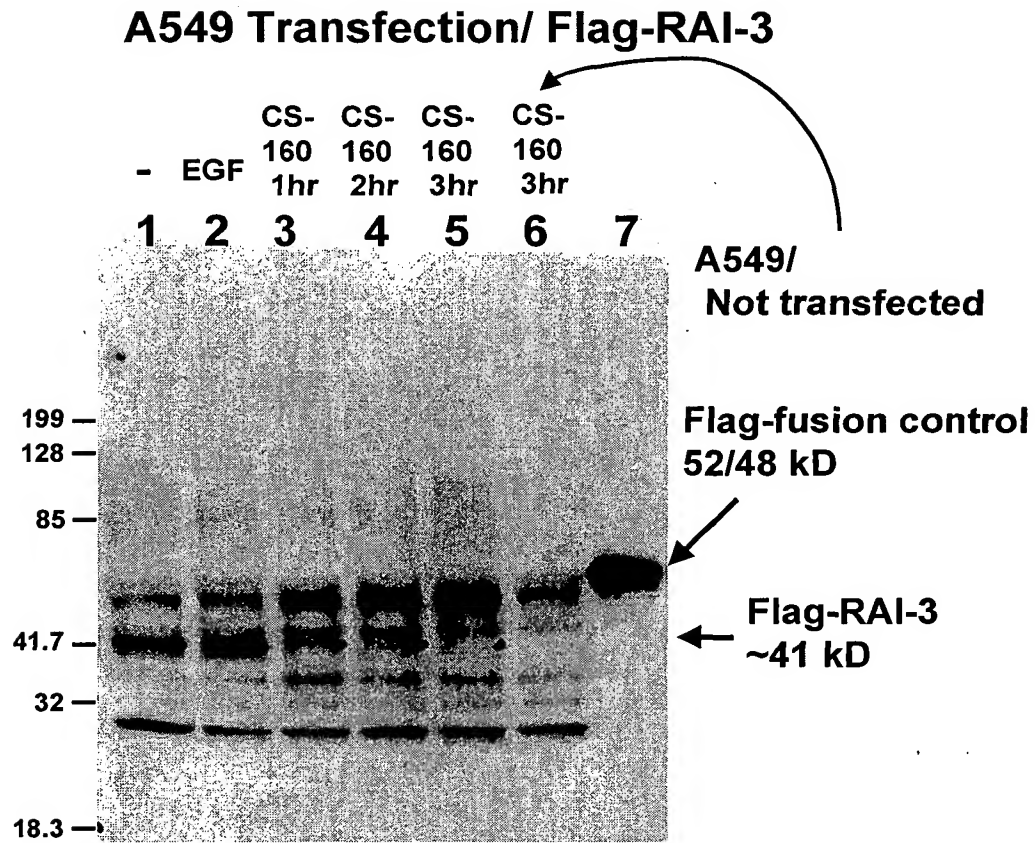


FIG. 26B

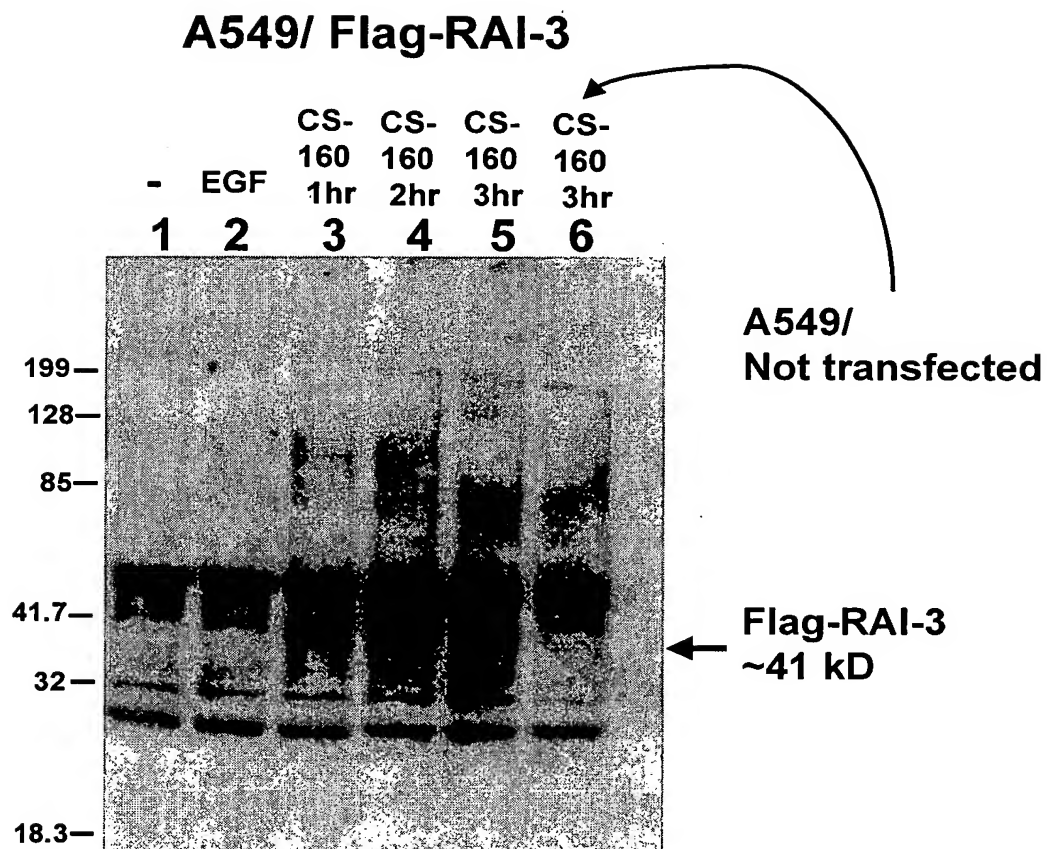


FIG. 27A

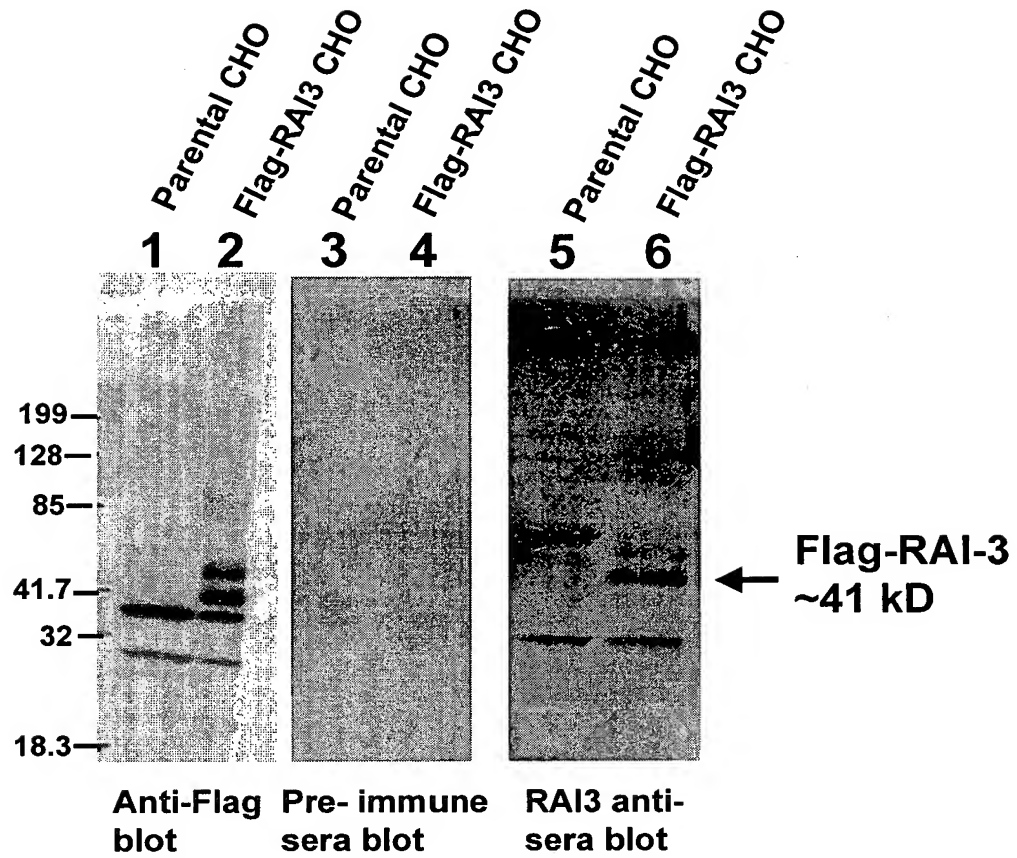
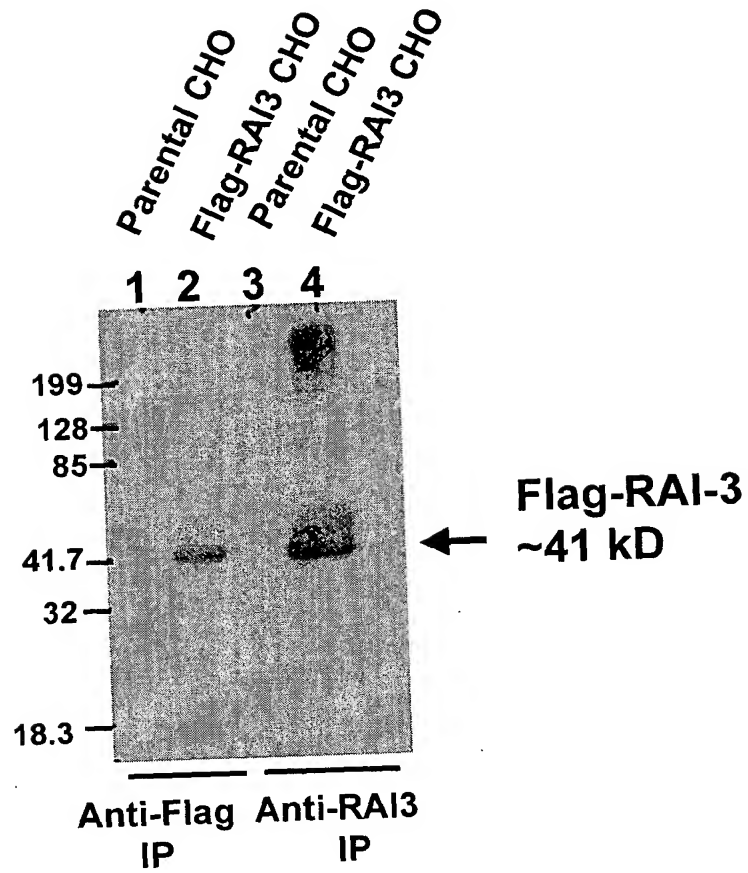


FIG. 27B



**FIG. 28A**

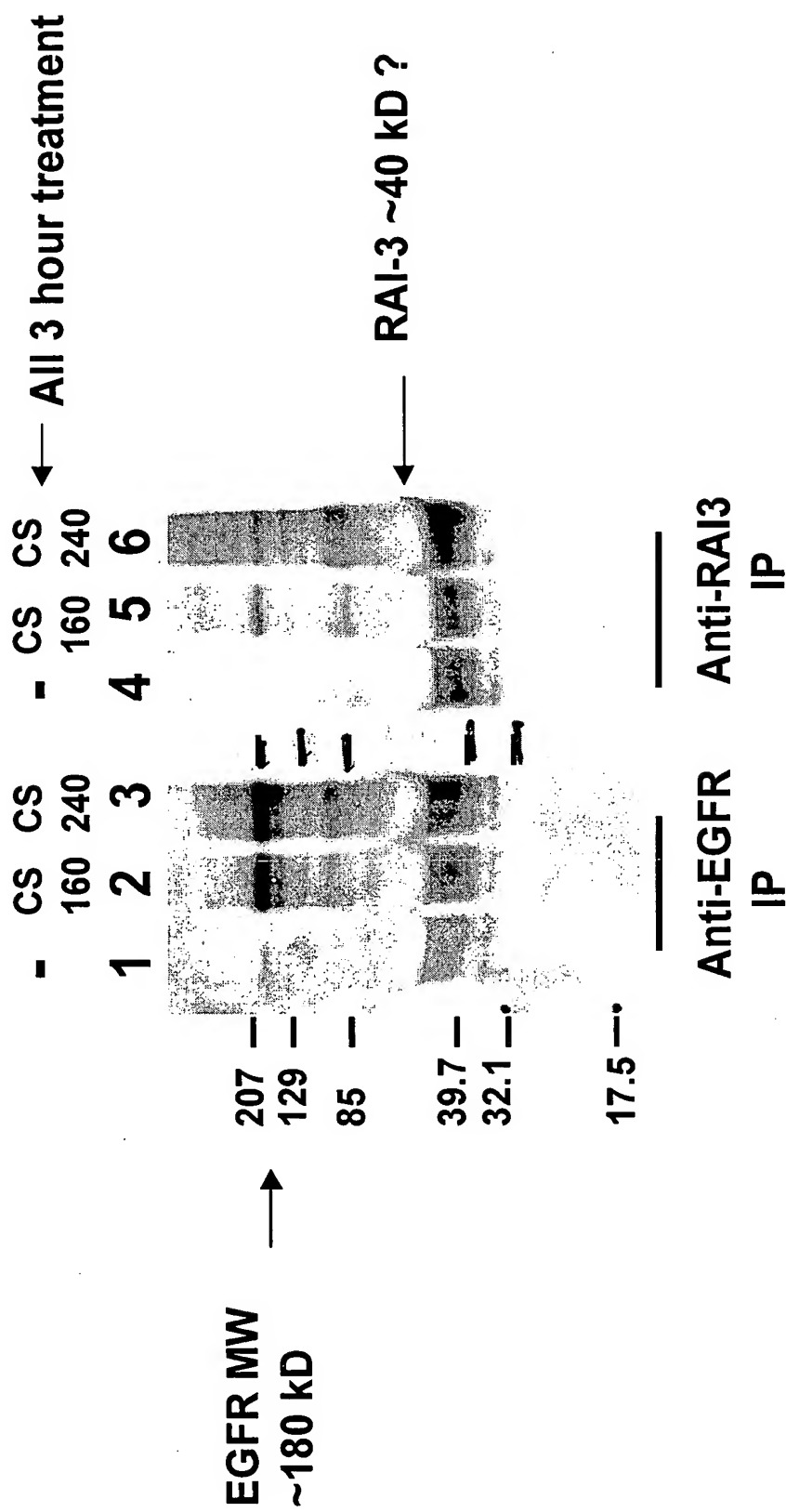


FIG. 28B

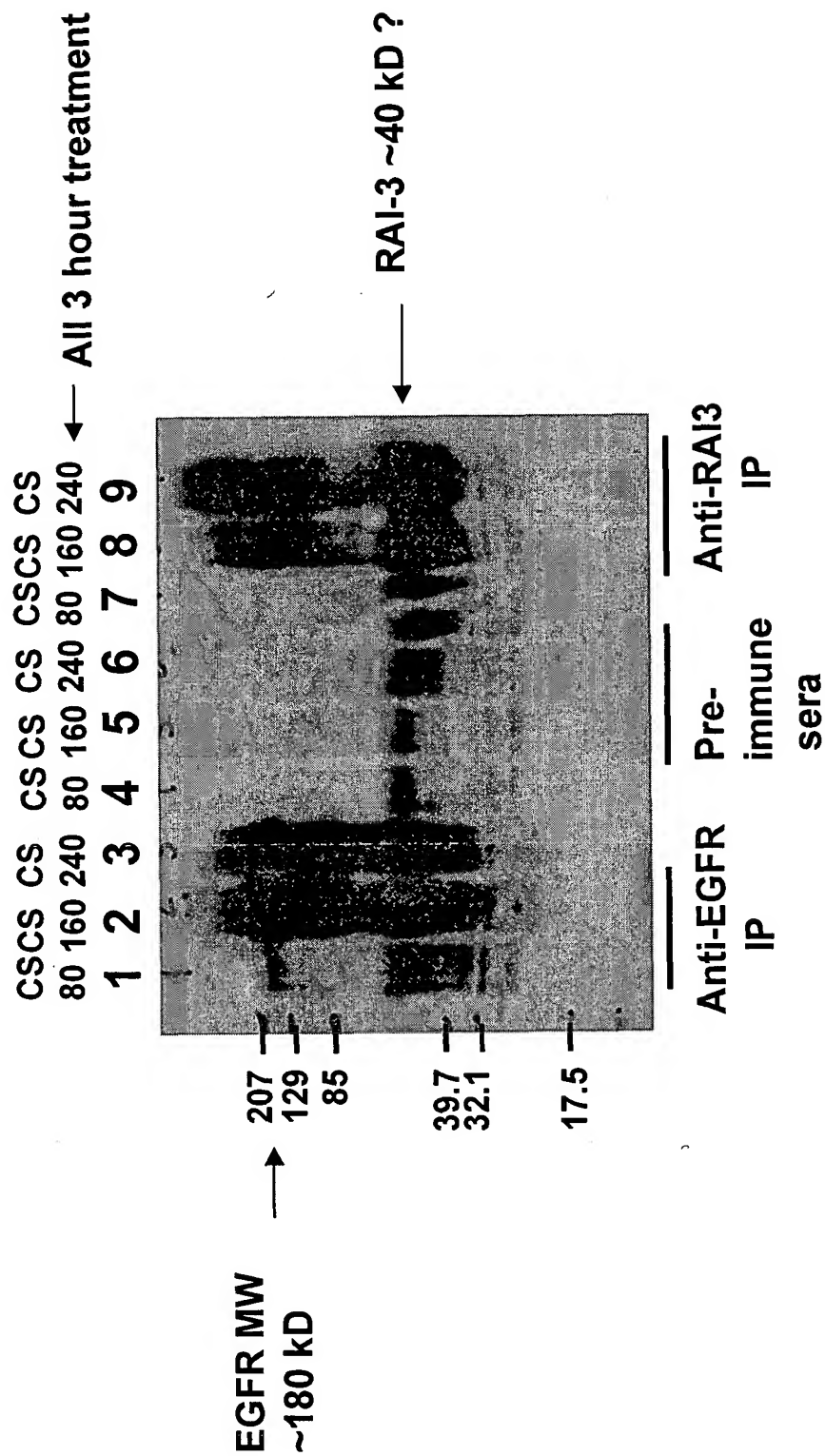


FIG. 29

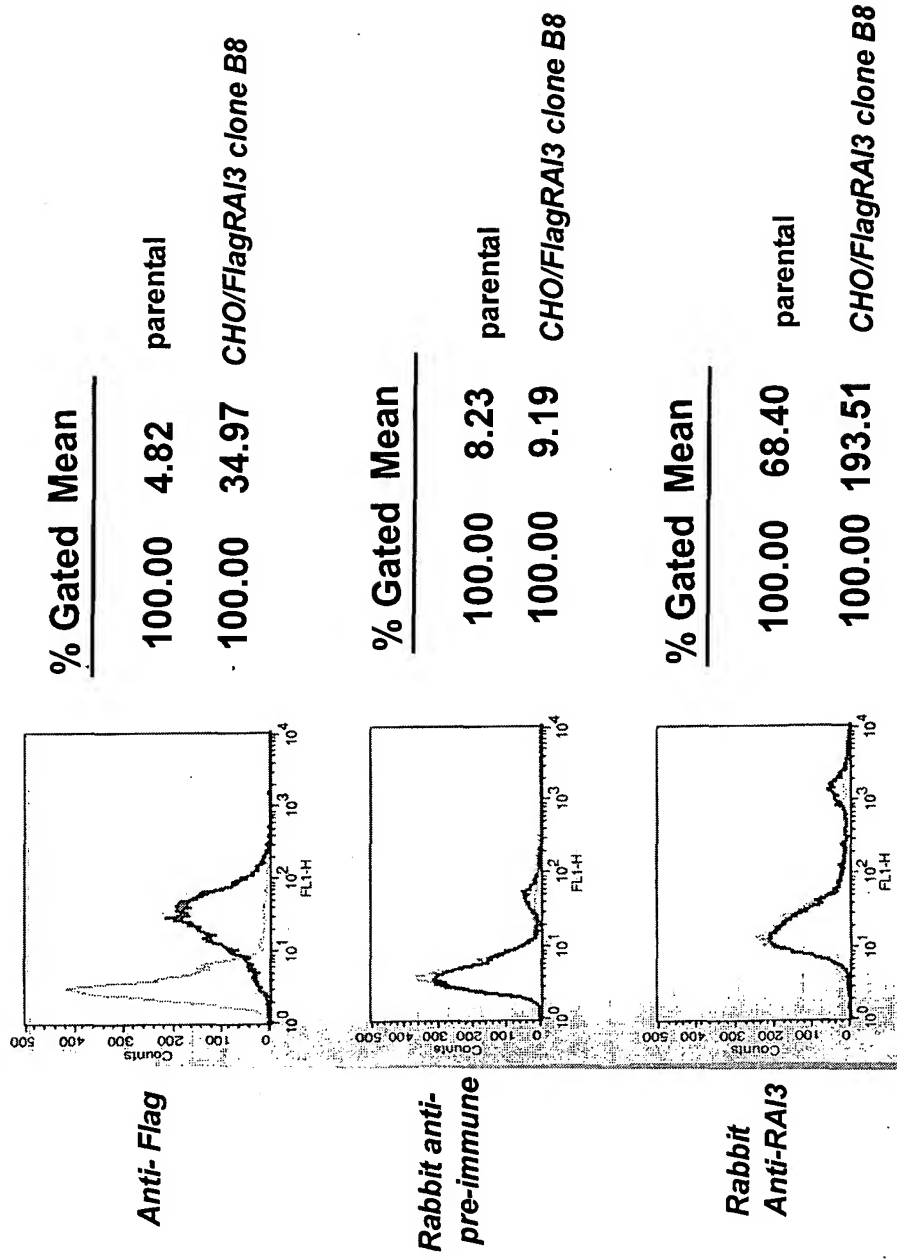


FIG. 30

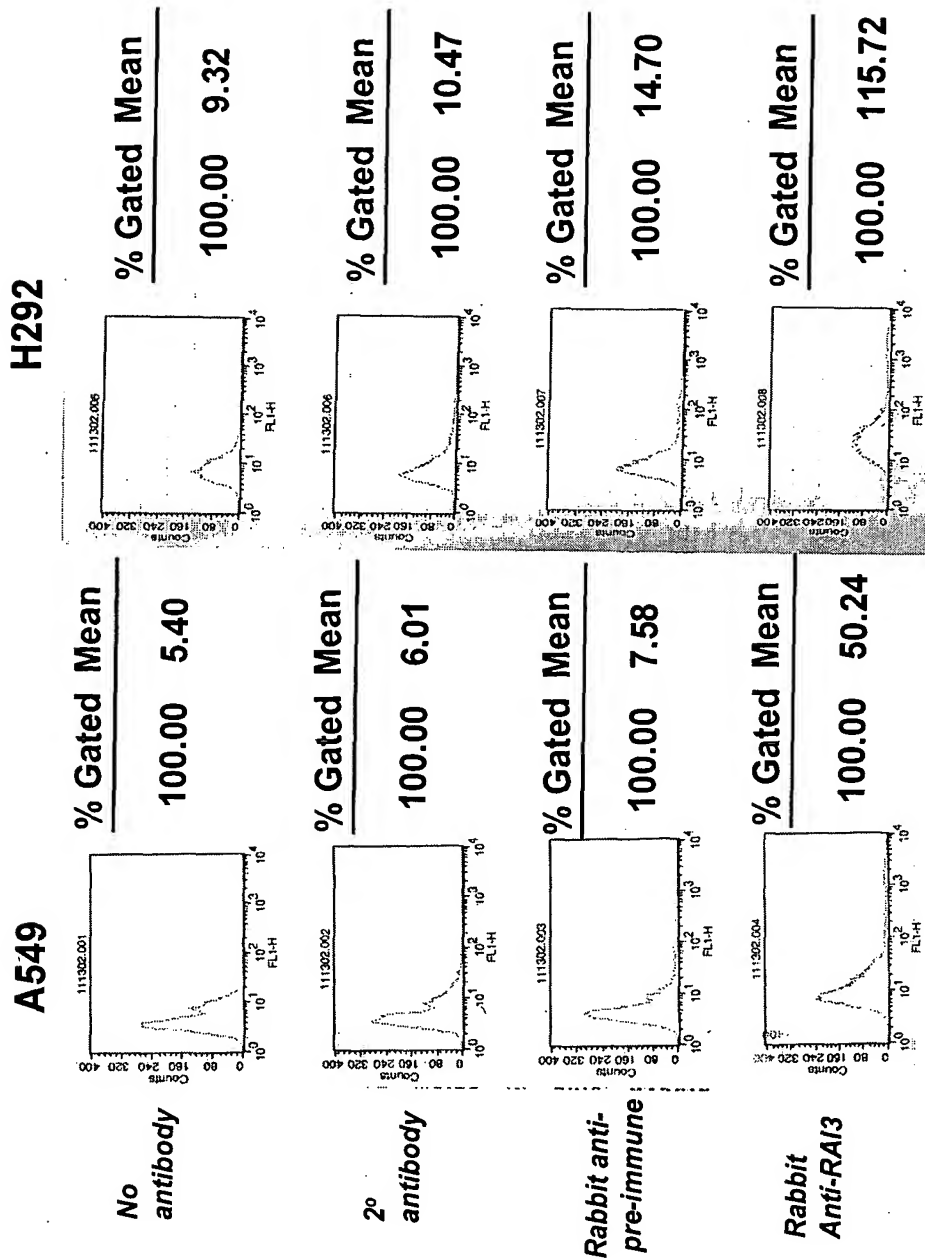
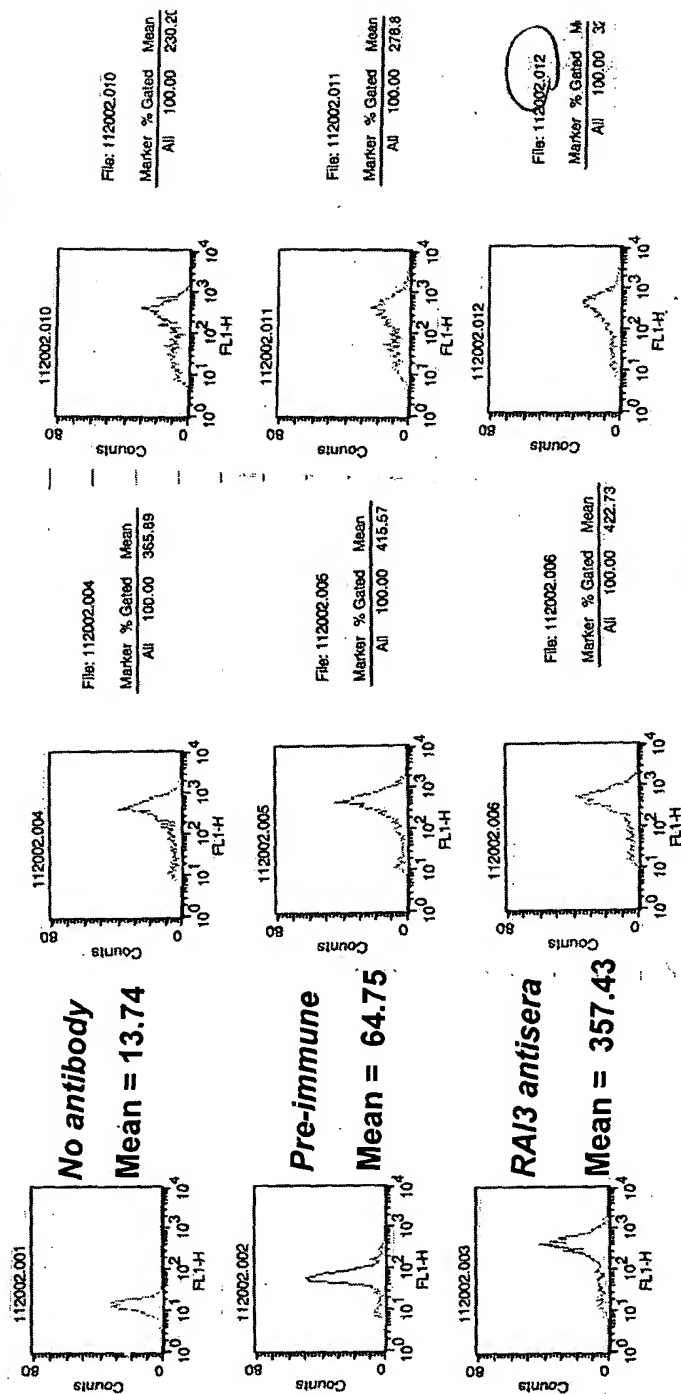




FIG. 31

**Not transfected**      **Lipofectamine 2000**      **1864 +1865**  
**with no siRNA**      **RAI3 siRNA**

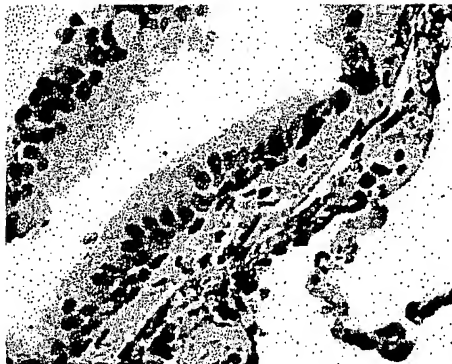


Ave Mean = 401

Ave Mean = 278.22

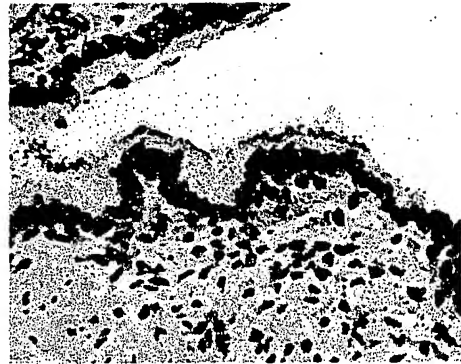
**FIG. 33**

**A. Normal Lung Tissue**



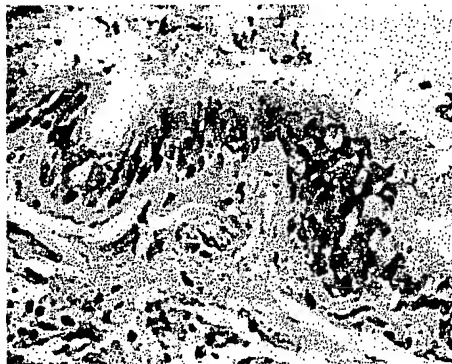
Respiratory Epithelium, Normal Lung

**B. Normal Lung Tissue**



Respiratory Epithelium, Normal Lung

**C. Emphysema, Human Lung Tissue**



Respiratory Epithelium, Emphysema

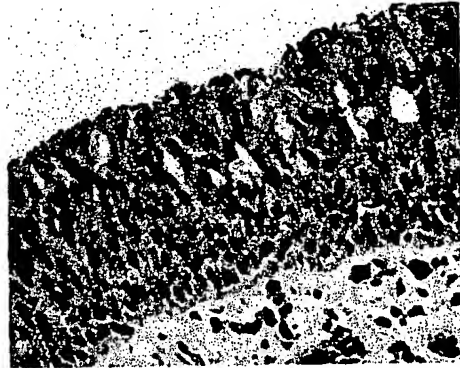
**FIG. 34**

**A. Chronic Bronchitis, Human Lung Tissue**



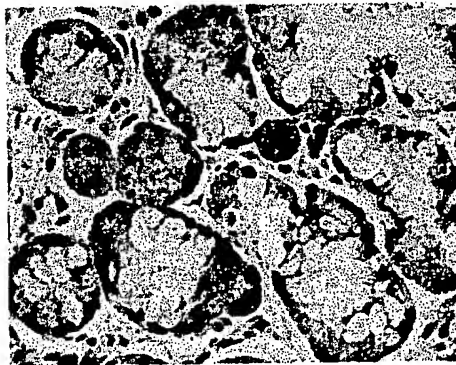
**Respiratory Epithelium, Bronchitis**

**B. Chronic Bronchitis, Human Lung Tissue**



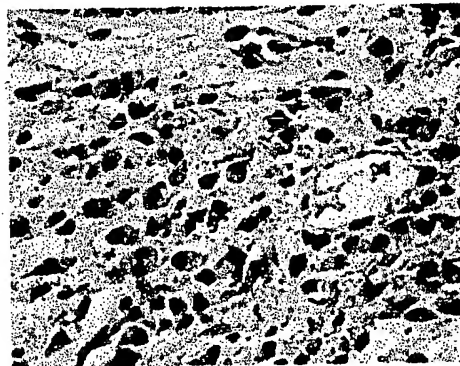
**Respiratory Epithelium, Bronchitis**

**C. Chronic Bronchitis, Human Lung Tissue**



**Seromucous Glands, Bronchitis**

**D. Chronic Bronchitis, Human Lung Tissue**



**Mucosal Inflammation, Bronchitis**

FIG. 32

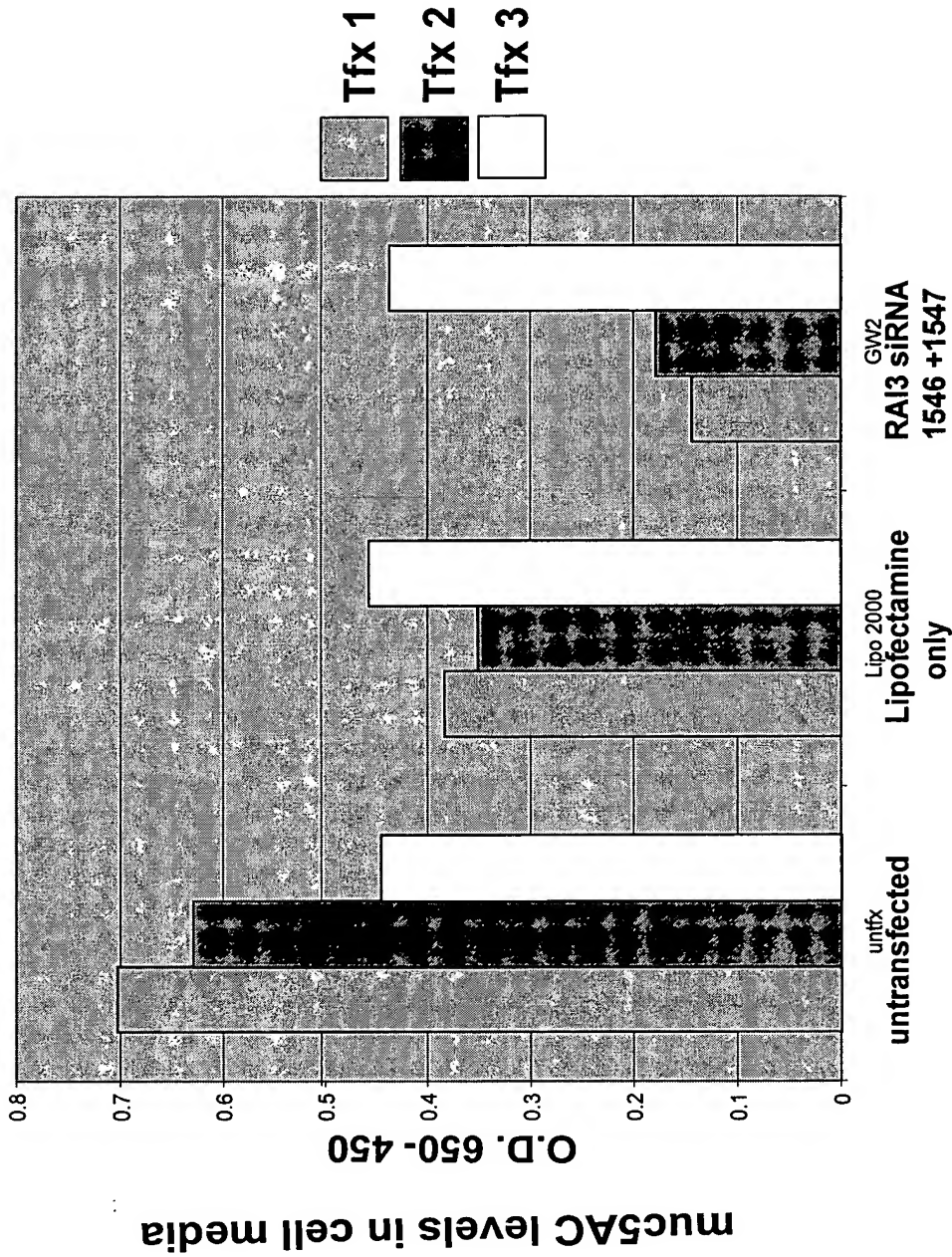
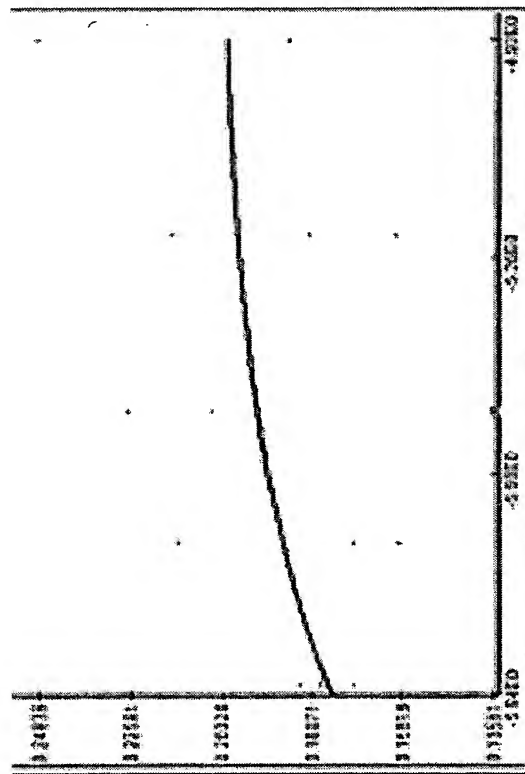


FIG. 35

A.



B.

